Research Paper

The Comparable Effect of tDCS and Core Exercises on Balance and Mobility in Patients With Multiple Sclerosis

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ABSTRACT

Objectives: As a major feature of the disease, motor-related complications, including loss of balance and reduced ability to walk were seen in multiple sclerosis (MS). The purpose of this study was to investigate the effect of core stability exercises and transcranial direct-current stimulation (tDCS) as a non-invasive brain stimulation on balance, walking capacity, and quality of life in patients with MS.

Methods: In this randomized clinical trial study with a pretest-posttest design, 29 female patients with an Expanded Disability Status Scale (EDSS) of less than 4.5 (3.75±1.31) and a mean age of 38.36±7.99 years were purposefully selected from patients referring to MS society of Tehran during 2021 and then randomly assigned to the following three groups: core stability exercises, anodal tDCS, and sham. Variables, such as balance, walking capacity, and quality of life were measured before and after the interventions. Subjects in the core stability training group participated in core stability exercises for three weeks, and subjects in both sham and anodal tDCS groups received direct brain electrical stimulation for five sessions.

Results: A significant improvement in balance and walking capacity were seen both in the anodal tDCS and the core stability training groups ($P<0.05$). Moreover, mobility was significantly changed in the tDCS group ($P<0.05$). However, no significant difference in the quality of life was seen between the groups.

Discussion: Our findings indicate comparable effects of tDCS, and core stability training on balance and walking capacity in patients with MS. Therefore, in addition to exercises, tDCS can be considered a promising tool for the neurorehabilitation of patients with MS.

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Highlights

• Our findings showed a significant improvement in balance, mobility, and walking capacity in the anodal tDCS group.

• Moreover, our results presented the positive effect of core stability training in balance and walking capacity, but not on the mobility of MS patients.

Plain Language Summary

Multiple sclerosis (MS) is the most common inflammatory disease of the central nervous system (CNS) that often results in disability in young adults. Unilateral weakness as a common clinical feature of dysfunction of the lower limb muscles may cause walking problems that require walking aids within 15 years of MS onset. Many common disabling symptoms, such as loss of balance, mobility dysfunction, and falling, cannot be fully controlled by medical treatment. The physical rehabilitation of MS patients needs a multidisciplinary approach that takes novel intervention methods into account as well. The present study investigated the effects of transcranial direct-current stimulation (tDCS) and core stability exercise on balance and functional mobility (assessed by the Berg balance scale and timed up and go test), walking endurance (assessed by a 6-minute walk test), and quality of life in patients with MS. Our findings showed a significant improvement in balance, mobility, and walking capacity in the anodal tDCS group and in balance and walking capacity in core stability training compared to the sham tDCS group.

1. Introduction

Multiple sclerosis (MS) is one of the common chronic and demyelinating diseases of the central nervous system (CNS) that often results in disability in young adults [1]. MS is a complex and clinically heterogeneous disease of the CNS with different neurological deficits related to the location and extent of neurologic lesions. Impairment of the sensory system, pyramidal tract dysfunction, and gait abnormality is commonly seen in MS [2]. Unilateral weakness as a common clinical feature of dysfunction of the lower limb muscles may cause walking problems that require walking aids within 15 years of MS onset [3]. Moreover, other functional impairments, including altered postural control, poor balance, and fatigue reduce the individual's ability to perform daily activities [4]. Activity restriction is mainly seen as a fall-related injury (reported in more than 50% of people with MS) that leads to disability and death, especially in older populations [5]. Many common disabling symptoms, such as loss of balance, mobility dysfunction, and falling, cannot be fully controlled by medical treatment [6]. Besides medical treatments, physical therapy strategies seeking to improve muscle strength and endurance are essential for preventing as well as rehabilitating motor dysfunction in patients with MS [7]. Individuals with MS tend to have reduced trunk stability [8]. Core stability plays an effective role in the improvement of balance and mobility in ambulant MS patients [9, 10]. But in general, there is limited evidence regarding the effectiveness of symptom-oriented treatment plans, including exercise, which prompts the search for novel effective methods of MS rehabilitation that are accessible, safe, and easy to administer.

Transcranial direct current stimulation (tDCS) is a non-invasive, easy-to-use, and inexpensive, brain stimulator that modulates cortical activity by using weak electrical current. In this technique, the current direction of cortical excitability is changed resulting in the enhancement of neural plasticity [11]. Multiple stimulation sessions show greater and more persistent effects, making it an efficient tool for treatment. Several studies have recently shown that tDCS produces neuroplastic changes for a long time, suggesting the potential therapeutic effects of the technique [12, 13]. TDCS is now being widely used to study cognitive and motor functions in healthy individuals as well as patients with neurological disorders. Using tDCS improves symptoms of neurological diseases, including Parkinson's disease (PD) [14], limb paresis after stroke [15], post-stroke aphasia [16], cognitive function in stroke patients [17], and dystonia [18]. In recent years, tDCS has been increasingly used in clinical trials on MS patients to ameliorate motor function [19], gait impairments [20], fatigue [21], difficulty swallowing [22], pain perception and sensory deficits [15], and cognitive function [23]. Although impaired walking and immobility interfere with the patient's independence and ability to complete daily activities [3], the tDCS effect on these symptoms of MS has been investigated in a few studies [24].

Previous single-session tDCS studies in MS patients have shown no significant effect on gait [20], walking speed, and functional mobility [24]. Nonetheless, multi-session tDCS on the lower limbs (in front of CZ) showed increased walking speed without a significant effect on daily mobility [25]. In a recent study, gait speed and distance improvement was reported by multi-session tDCS applied over the motor cortex [26]. Considering that lower limb disability is commonly reported in patients with MS [27], which leads to dysfunction in balance, mobility, and walking, investigating the effect of non-pharmacological interventions on motor symptoms in MS patients appears crucial. Thus, the first goal of the present study was to investigate the effect of core stability training on these dysfunctions.

Despite recent studies on the tDCS effectiveness on walking capacity, there is a lack of ample evidence about the effects of tDCS on balance in patients with MS. Gathering data on the potential benefits of this modality might offer a new treatment option to patients with MS. Considering the importance of treating balance and walking impairment in patients with MS, a preferential treatment strategy should be specified. Thus, the second goal was to assess the effect of tDCS on these symptoms. Finally, comparing the effect of tDCS with physical training targeting core stability as two rehabilitation methods for people with MS was another goal of our study.

2. Materials and Methods

Participants

A randomized clinical trial study with a pre-test-post-test design was conducted, which included patients referring to the MS society of Tehran in 2021. All the participants whose diseases were confirmed by a neurologist were recruited using a convenience sampling method. All patients continued receiving their regular medications during the study. All the participants met McDonald's criteria for MS disease [28] and the course of the disease and symptoms had remained stable for at least one month prior to the study. Patients with a new neurologic episode during the month preceding the study, a history of head trauma, neurological comorbidity (stroke and seizure), chronic psychiatric disorders, alcohol or drug abuse, and treatment with brain stimulants (such as methylphenidate and amphetamine) were excluded. The subjects were randomly assigned to one of three groups by drawing concealed envelopes from a box: The core stability training group (n=10, mean age= 40.20±7.69 years), the anodal tDCS (A-tDCS) group (n=9, mean age= 37.44±7.89 years), and the sham tDCS (S-tDCS) group (n=10, mean age= 37.70±7.78 years).

Functional balance and mobility, walking capacity, and quality of life were assessed (see the assessment section for more details). The assessments were completed at baseline (pretest) immediately before the first session and after the end of the intervention sessions (posttest) just after the last session (Figure 1).

Interventions

Core stability training

The intervention included individualized, face-to-face, core stability training exercise sessions (30 minutes, delivered three times per week over six weeks), plus a daily 15-minute home exercise program for each patient [10]. The core stability exercises were selected from a package (including balance exercises to strengthen and activate the stabilizing muscles), each with two or three levels of difficulty in accordance with each participant's physical capacity. The exercise training was performed under supervision. Stretching was performed before or during the exercises. The exercise protocols were designed to progressively challenge trunk control [9] (Table 1). The progression of the exercises corresponded with each individual's abilities.

TDCS stimulation procedure

TDCS was used for electrical stimulation (delivered by ActivaDose) with saline-soaked sponge pads of 5×5 cm2. The stimulation was applied under the supervision of a specialist through the anode electrode over the M1 cortex (10% to 20% anterior to CZ in the midline in

Figure 1. Diagram of the intervention protocol.

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BBS: Berg Balance Scale, TUG: Timed Up and Go, QOL: Quality of life, 6-min W: 6-minute walk test, CST: Core stability training

Table 1. Core stability exercise

Core Stability Exercise	Base Level	Level 1	Level 2	Level 3
Table top	×	×	×	
4-Point Kneeling	×	×	×	×
Forward Bend		×	×	
Bridge		×	×	
One Leg Stretch		×	×	
Backward Lunge		×	×	
Bent Leg Side Lifts		×	×	
Single Leg Drop Out		×	×	
Horizontal Hold	×	×	×	
Straight Leg Side Lifts		×	×	
Knee Rolling on Gym Ball				
Bridging on Gym Ball		×	×	
Arm Lifts		×		
Arm Sweeps		×		
Head Lifts		×		

Using overload principle in every session with minimum 8 repetition

Iranian Rehabilitation Journal

accordance with the international 10-20 EEG System) while the cathode electrode was located over the left supraorbital area to enhance the activation of the cortical pathways [29]. This montage of stimulation was chosen in the present study to increase cortical excitability in the lower limbs of both hemispheres. For the anode (active) group, an electric current of 2mA was given for 20 min once a day (in the morning) for five consecutive days [30]. For the sham group, the electric current was turned off 60 sec after the stimulation onset [31]. This sham tDCS method had no considerable neuromodulatory effects but elicited similar sensations that were produced by real tDCS stimulation. It should be emphasized that the control group did not undergo any training or stimulation affecting their motor ability.

Assessments

Functional balance: The functional balance was assessed using Berg Balance Scale (BBS). This scale rates the patients' performance in 14 common daily living tasks (e.g. sitting, turning, and picking up objects) from 0 (worst) to 4 (best) [32].

Functional mobility: Functional mobility was measured using the Timed Up and Go (TUG) test as a highly reliable tool for assessing mobility in individuals with MS [33]. This test measures the time needed for the respondent to get up from a sitting position, walk a distance of 3 meters, return, and sit down again (less time consumed to perform this task equals better performance) [32].

Walking capacity: A 6-minute walk test was used to assess walking capacity. For this test, the subjects started walking with the verbal command of the examiner (no running was allowed), and the distance traveled was measured after 6 minutes [33]. All the functional evaluations were timed with a digital timer. Roberta Rikli et al. reported the validity of this test as 0.88 to 0.94 and its reliability as 0.71 to 0.82 [34].

Quality of life: The subjects' quality of life was assessed using the 54-item MS Quality of Life (MSQOL-54) questionnaire consisting of 14 parts, each part with several questions covering different aspects of life, including physical function, role limitations-physical, role limitations-emotional, pain, emotional well-being, energy, health perceptions, social function, cognitive function, health distress, sexual function, change in health, satisfaction with sexual function, and overall quality of life. To calculate the subjects' scores in this questionnaire, each of the 14 parts was first separately given a score from 0 to 100, and the average of the 14 sections was then calculated as the measure of QOL. This questionnaire has been developed by Vickery et al. and is widely used for MS patients because of its validity and reliability [35].

Statistical analysis

We had no missing data in the assessments or performances of the groups. The Shapiro-Wilk normality test was performed to detect the normality of variables. A dependent t-test was used to compare within-group variables. In addition, regarding the homogeneity of variance and regression slope, multivariate analysis of covariance (MANCOVA) was conducted to compare differences between post-test scores of three groups, using baseline values as covariates. If the results were significant, the Bonferroni test was used. The p-value level below 0.05 was defined as significant. The effect size was measured by partial eta-squared (η^2). We performed statistical analysis using IBM SPSS software, version 19.

3. Result

There were not any drop-outs from the trial and all of the participants completed the tests. Participants did not complain of any headache or discomfort. However, they did not know whether they were receiving sham or active tDCS. The demographic characteristics of participants in each of the three groups (A-tDCS, S-tDCS, and core stability exercise) are presented in Table 2.

The results for the self-report assessment (quality of life) and performance parameters (time up and go, six-minute walk, and Berg balance test) for each group are presented in Table 3. A significant difference was observed between all pre- and post-intervention evaluations (time up and go, six-minute walk, Berg balance test, and QOL) in the A-tDCS group ($P<0.05$) and in pre- and post-intervention performance assessments (time up and go, six-minute walk, and Berg balance test) in the core stability group ($P<0.05$) but not in the S-tDCS group.

Regarding homogeneity of variance and regression slope, multivariate analysis of covariance (MANCOVA) was conducted to compare the post-intervention results of groups, using baseline values as covariates (Table 4 and 5).

Table 2. Participant's demographic descriptive information in each of the groups

Variables		Mean±SD / No. (%)		
		A-tDCS	S-tDCS	Core Stability Exercise
Age (year)		37.44±7.89	37.70±7.78	40.20±2.43
Body mass index (BMI)		21.33±1.15	22.43±3.12	21.90±3.35
History of MS (year)		9.44±4.30	9.90±6.90	9.50±7.32
Expanded Disability Status Scale (EDSS) score		3.33±1.75	3.85±1.08	4.35±1.15
Education	Diploma	3(33.3)	2(20.0)	2(20.0)
	Bachelor's degree	3(33.3)	3(30.0)	3(30.0)
	Master's degree	2(22.2)	4(40.0)	5(50.0)
	PhD	1(11.1)	1(10.0)	0(0)

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A-tDCS: anodal transcranial direct-current stimulation; S-tDCS: sham transcranial direct-current stimulation

Table 3. Descriptive indicators of pre- and post-intervention evaluations of the groups

Groups	Variable	Pre-Test	Post-Test	t	P
A-tDCS	Time up and go	8.98±2.78	6.62±1.81	4.35	0.002
	Six-minute walk	203.22±76.12	238.88±70.04	4.97	0.001
	Berg Balance	34.00±4.74	39.33±4.71	18.47	0.000
	Quality of life	63.15±8.32	62.15±8.23	3.207	0.012
S-tDCS	Time up and go	7.66±0.96	7.78±1.30	0.743	0.476
	Six-minute walk	233.4±39.92	234.6±48.77	0.296	0.774
	Berg Balance	41.7±5.65	41.7±6.25	0.000	1.000
	Quality of life	60.58±13.50	59.97±12.83	1.21	0.254
Core stability exercise	Time up and go	7.23±1.25	6.78±1.28	3.91	0.004
	Six-minute walk	187.2±38.64	215.9±40.36	9.46	0.0001
	Berg Balance	38.7±4.66	42.00±4.34	11.00	0.0001
	Quality of life	62.72±8.49	62.69±8.99	0.212	0.837

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A-tDCS: anodal transcranial direct-current stimulation; S-tDCS: sham transcranial direct-current stimulation

Regarding the results of MANCOVA on time up and go performance, a significant main group effect ($F_{[2]}$=27.442, P=0.0001, η^2=0.714) was seen (Table 4). Post-hoc tests revealed a significant difference between the A-tDCS group and the core stability group (P=0.0001) and the S-tDCS group (P=0.0001). It should be noted that there was no significant difference between the core stability and S-tDCS groups (P=0.197).

Considering the results of MANCOVA on a six-minute walk, a significant main group effect ($F_{[2]}$=22.54, P=0.0001, η^2=0.672) was seen (Table 5). Post-hoc tests revealed a significant difference between the A-tDCS and the core stability group (P=0.012) and the S-tDCS group (P=0.0001). There was also a significant difference between the core stability group and the sham group (P=0.01).

Table 4. The result of MANCOVA using pre-tests values as covariates

Variable	Value	F	P	η^2
Pillai's Trace	1.279	384.969	0.0001	0.639

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Table 5. Results of multivariate analysis of covariance to investigate differences in three study groups

Variables	Sum of Squares	df	Mean Square	F	P	η^2
Time up and go	24.992	2	12.496	27.422	0.0001	0.714
Six-minute walk	7404.82	2	3702.41	22.54	0.0001	0.672
Berg Balance	98.192	2	49.096	43.768	0.0001	0.799
Quality of life	3.456	2	1.728	1.186	0.324	0.097

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Considering the results of MANCOVA on the Berg balance test, a significant main group effect ($F_{[2]}$=43.768, P=0.0001, $η^2$=0.799) was found (Table 4). Post-hoc tests revealed a significant difference between the A-tDCS and S-tDCS (P=0.0001) groups. There was also a significant difference between the core stability group and the sham group (P=0.0001). It should be noted that there was no significant difference between the A-tDCS and core stability groups (P=0.072).

Finally, according to the results of MANCOVA on quality of life as a self-report measure, no significant group effect ($F_{[2]}$=1.186, P=0.324, $η^2$=0.097) was seen.

4. Discussion

The present study investigated the effects of tDCS and core stability exercise on balance and functional mobility (assessed by the Berg balance scale and TUG test), walking endurance (assessed by a 6-minute walk test), and QOL in patients with MS. Our findings showed a significant improvement in balance, mobility, and walking capacity in the anodal tDCS group and in balance and walking capacity in core stability training compared to the sham tDCS group. Meanwhile, none of the interventions were found to positively affect the QOL. In addition, our findings showed a significant difference between the effects of anodal tDCS and core stability exercises on walking capacity.

Improvements in motor function in patients with cortical and subcortical lesions as well as patients with impaired balance by administration of tDCS over the primary motor cortex were previously reported [36]. Our findings are consistent with the results of previous studies, which have demonstrated the beneficial effects of tDCS on balance and gait in leukoaraiosis [31], balance and fear of falling in Parkinson's disease [37], balance and strength of the affected extremity in stroke [38], walking and gait in stroke, gait in Parkinson's disease [39], and balance and gait in children with cerebral palsy. Similar to our investigation, most of these studies on tDCS targeted the motor area (in front of the CZ), corresponding to the lower limb region of the primary motor area (M1), in order to enhance lower limb motor function, balance, and functional mobility. A possible mechanism of this effect could be that cortical excitability is facilitated, which in turn leads to an increase in the voluntary movement of the lower limb [40, 41]. The motor area stimulated by tDCS may increase corticospinal output and projection strength in patients with MS [42]. Neural excitations are a result of an increase in blood perfusion and functional connectivity enhancement within the sensorimotor cortex [43]. Moreover, some recent investigations applied tDCS over the motor cortex to improve gait in patients with MS [20]. Our results suggest that tDCS targeting the lower limb motor cortical regions, which are involved with balance and walking, may compensate for the cortico–subcortical disconnection caused by MS lesions. Studies have previously reported the excitation of the cortical leg area with tDCS leading to locomotor control improvement in healthy participants [44]. In the present study, stimulation was applied in the frontal region, in the midline, and in front of the CZ (according to the International 10/20 EEG System) in order to modulate the bilateral lower limb motor cortices.

In previous studies, in order to improve balance and walking in patients with MS, tDCS was administrated alone [20] or in combination with physical training [26]. In our study using tDCS and physical training as two separate interventions in different groups, findings showed that both core body exercises and tDCS improved balance in patients with MS, and there was no significant difference between their effects. Core body exercises improved balance and walking endurance by the excitation of the relevant motor areas that may affect corticospinal and intracortical networks [45], whereas tDCS achieved this outcome by lowering the threshold, which allowed for the same changes to occur [46]. It is worth noting that the methodology of the present multi-session tDCS study has been improved over that of recently-published research findings focused on the effect of tDCS in subjects with MS. In some recent investigations, the effect of exercise training along with tDCS has been evaluated [24, 25]. Single-session tDCS over the M1 did not improve walking and functional mobility in subjects with MS, which is different from our study using a multi-session intervention, and another single-session tDCS study also showed that the stimulation was more effective if applied before rather than during walking (as a paired intervention) [20], which is different from the present study, in which two interventions were performed separately. As a result, the authors decided to examine a multi-session intervention [24]. Most recently, a double-blind study using multi-session tDCS paired with physical exercises showed cumulative effects on walking parameters [26]. These authors focused on the left M1 cortex (C3 based on the 10-20 EEG system), which differs from our study, in which stimulation was applied in front of CZ in order to cover the bilateral motor cortex. The results of the present study showed that tDCS alone has beneficial effects on MS patients' balance, functional mobility, and walking endurance that are comparable with the effect of physical exercises.

Our findings showed that there was no significant difference between the effects of tDCS and physical training on QOL in patients with MS. In contrast, other studies have shown that QOL improved after multi-session tDCS targeting the prefrontal or primary motor area and performed to reduce fatigue or pain [47]. This may be due to differences in the intervention. In the present study, the subjects received tDCS stimulation on the M1 cortex (that stimulates motor function without effect on cognitive and psychological characteristics of patients) in the A-tDCS group. Even though depressed mood, fatigue, and disability status have the most impact on QOL in MS patients. On the other hand, subjects performed core body exercise (instead of aerobic exercise that produces a significant improvement in vitality and QOL) only for six weeks in the core exercise training group. The limitations of the present study include the relatively small sample size and the failure to investigate balance with an instrument. Such investigation can benefit from the use of an advanced system (such as the Biodex Balance System) to assess static and dynamic balances in the future. In addition, placing the anode electrode on the CZ and the cathode over the supraorbital area may stimulate multiple brain areas that contribute to balance control. This effect is explained by the relatively large size of the stimulation electrodes that may have influenced brain areas surrounding M1. Therefore, future studies are recommended to apply better-targeted stimulation and investigate alternative motor electrode montages. Another limitation of the present study was the participation of only female subjects.

To summarize, the present study showed that anodal tDCS over the motor area is a safe technique without any reported side effects that can be used in patients with MS with minimal side effects and no adverse effects. Our study is the first randomized, multi-session, sham-controlled trial that confirms the effect of tDCS on balance, mobility, and walking. This effect has also been compared with that of exercise in MS patients. Finally, the therapeutic effects of tDCS on balance, functional mobility, and walking endurance are promising for the neurorehabilitation of patients with MS.

5. Conclusion

Our findings indicate that tDCS over the M1 improves balance, functional mobility, and walking endurance in patients with MS. Nonetheless, these effects were not accompanied by an improvement in the patient's quality of life. Moreover, core body exercises can also improve balance and walking endurance except for functional mobility in patients with MS. In addition, our results did not show any significant differences in the observed effects of tDCS and core body exercises.

Ethical Considerations

Compliance with ethical guidelines

Ethical principles were considered in this article. This study was approved by the biomedical research ethics committee of the University of Tehran (IR.UT.SPORT.REC.1400.051). All the participants provided written informed consent to participate in the study and they were informed of the purpose of the research and its implementation stages.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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