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Effects of Transcranial Direct Current Stimulation on Different Electrode Sites on the Activity of the Upper Extremity in Chronic Stroke Patients: a Randomized, Double-Blind, Sham-Controlled Trial

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This study examined the effects of transcranial direct current stimulation (tDCS) on different electrode sites on the activity of the upper extremity in chronic stroke patients. Forty-five subjects were randomly assigned to unilateral tDCS, dual tDCS, and control groups, and tDCS was applied to the unilateral tDCS and dual tDCS groups for 20 minutes per day, 5 times a week for a total of 4 weeks. The activity of the subject's upper extremity was evaluated by a hand grip strength test, an elbow flexor and wrist flexor muscle tone test, and a Jebsen Taylor hand function test. In the unilateral tDCS group, dual tDCS group, and control group, significant improvement was observed in the hand grip strength test and the Jebsen Taylor hand function test after intervention ($p<.05$), and there was significant improvement in the hand grip strength test and the Jebsen Taylor hand function test compared to the control group ($p<.05$). The results of this study suggest that tDCS applied to the primary motor cortex (M1) positively affects the activity of the upper extremity in stroke patients.

Keywords : transcranial direct current stimulation, electrode site, electromagnetic field, activity of upper extremity, stroke

1. Introduction

Stroke is a disease that causes impairment of motor and cognitive function and loss of sensation in the body on the side opposite to the damaged cerebral hemisphere, causing limitations in physical function and activity performance [1]. Especially when compared with the recovery of the performance of the lower extremities, the recovery of the performance of the upper extremities, with its many delicate movements such as gripping and manipulation, appears slow [2]. Upper extremity performance plays an important role in daily life and the occupational environment and is important in determining the quality of life of patients; therefore, treatment to restore it is very important [3].

The human brain has plasticity: the ability to undergo structural and functional changes, as a result of various inputs from its internal or external environment over its lifetime [4]. Brain plasticity is associated with the increased excitability of the cerebral cortex and synaptic efficiency, which is highly correlated with motor function. In other words, there is no kinetic change without brain neurological change [5]. As such, various physical therapy methods, such as constraint-induced movement therapy (CIMT) and task-oriented therapy, are used to stimulate the plasticity of the brain in stroke patients and to restore activity performance.

Recently, studies have been attempted to promote the recovery of function in brains impaired by nervous system diseases by directly modulating brain functions rather than through treatments that indirectly affect the brain through exercise therapy [6]. Transcranial direct current stimulation (tDCS) is the most representative noninvasive device that can directly stimulate the brain and change the excitability of brain cells by promoting or suppressing the excitability of the living human brain. It is used to restore the performance of activity due to brain disease [7]. During tDCS, two electrodes are attached to the scalp, and they create a small current of about 1–2 mA, which increases the excitability of brain nerve cells at the anode electrode and decreases excitability at the cathode electrode [8].

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The effect of tDCS on activity performance has been demonstrated in many studies. The application of an anode electrode to the primary motor sensory and premotor areas can enhance the motor function of the hand and promote implicit motor learning and working memory, and to the motor cortical area. It has been reported that the application of transcranial direct current increases the amplitude of the motor evoked potential by promoting the excitability of cortical spinal cord neurons [9, 10]. While many studies have been conducted on the effect of an anode electrode on tDCS, research on the effects on a cathodal electrode is still insufficient [11]. The positive electrode, which increases the excitability of cranial nerve cells, is attached to the primary motor area (M1) of the injured brain hemisphere, and the negative electrode, which suppresses excitation, is attached to the primary hemisphere of the undamaged brain hemisphere. The activity of the brain hemispheres on the injured side is measured [12]. Therefore, the purpose of this study was to investigate the effect of tDCS on both brains, to find out how it affects the upper extremity performance of stroke patients during bilateral and unilateral brain stimulation, and to confirm the relevance of stroke activity. This will, in turn, contribute to understandings of neurophysiological mechanisms.

2. Materials and Methods

2.1. Participants

The subjects in this study were patients diagnosed with hemiplegia due to unilateral brain injury following a stroke, they were hospitalized for chronic hemiplegia more than three months after onset. After receiving an explanation of the purpose and procedure of the study, 45 patients with stroke who agreed to participate were selected. Of the 45 stroke patients who participated in the experiment, 10 were excluded from the experiment due to dizziness, and 35 completed the experiment. The specific selection criteria are as follows: their right hand is dominant (according to the Edinburg handedness inventory), the patient suffered damage to the left hemisphere and not to the primary motor area (M1), they have a score of 1–2 on the Modified Ashworth Scale (MAS) of the upper extremity, they do not have a visual impairment and can communicate, and they have not participated in an experiment in the last three months that exerted external stimulation on the cerebral cortex.

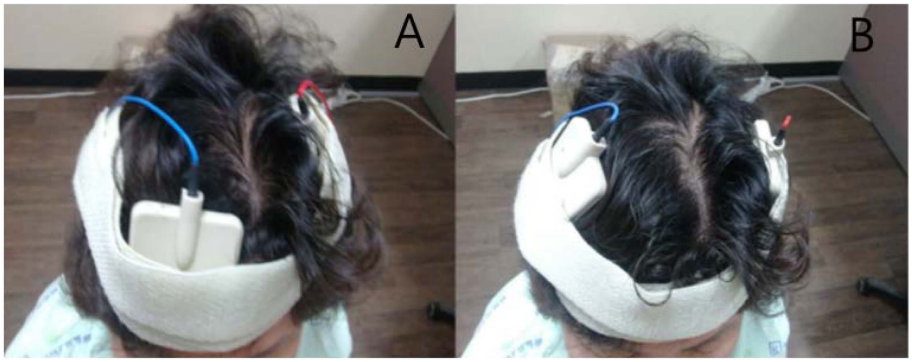
2.2. Study design

For the 45 patients meeting the selection criteria, 15 patients were randomly designated the unilateral hemisphere M1 tDCS group, 15 were designated the dual hemisphere M1 tDCS group, and 15 were designated the sham stimulation group. An evaluation of upper extremity function was performed for all subjects before tDCS application, four weeks after tDCS, and two weeks after therapy. In addition, all evaluations were conducted using a double-blind, randomized, sham control design that anonymized the patients randomly assigned to the three groups.

Fig. 1. (Color online) Transcranial direct current stimulation.

2.3. Intervention

All of the subjects were treated with tDCS for four weeks while sitting comfortably on a chair with a backrest. The transcranial direct current stimulator used was the Phoresor II Auto (Model PM 850, IOMED, USA) (Fig. 1), and it used a sponge moistened with saline on two electrodes made of 5 × 7 cm rubber. Thus, a current of 1 mmA was energized for 20 minutes. The total amount of current was conducted at 0.029 mA/cm², which did not damage biological tissue. According to the specifications of the 10/20 international electroencephalographic system of EEG measurement, the anode electrode was placed on the left hemisphere primary motor area (C3) of the left hemisphere (Fig. 2). The C3 region is a region corresponding to the primary motion sensory region; it controls the activity of the upper extremity from the central zero (Cz) to the outside at 5 cm. The cathodal electrode is a reference electrode in the unilateral brain stimulation group; it is attached to the supraorbital area of the right hemisphere. In the bilateral brain stimulation group, the right hemisphere primary motor area of the undamaged brain hemisphere was attached on the C4 site (Fig. 2). In the placebo stimulation group, the same stimulator was used, but no current was applied. All subjects performed a gripping exercise using a sponge ball while the transcranial direct current electrical stimulation was energized.



A. Unilateral tDCS B. Dual tDCS

Fig. 2. (Color online) Montage of tDCS application.

2.4. Outcome measure

2.4.1. Hand grip strength test

The hand grip strength test was performed using an electronic dynamometer (digital hand dynamometer, 5030KIT, Preston, USA) (Fig. 3). The measurement posture was adduction by keeping the shoulder joint close to the torso in a sitting position on the chair, flexing the elbow joint at 90°, and leaving the forearm neutral. The test was conducted in this posture with the arm on the table to minimize fatigue.

2.4.2. Modified Ashworth Scale

The MAS is the most commonly used six-step scale among clinical evaluation methods for stiffness. This study examined the effected wrist and elbow joints. In MAS level 6, grade 0 has no increase in muscle tone, grade 1 has a slight increase in muscle tone (ROM end range), grade 1+ has a slight increase in muscle tone (ROM less than 1/2), and grade 2 has the highest range of joint motion. The muscle tone is significantly increased, but manual joint exercise is easy. Grade 3 indicates difficulty in manual joint movement due to a severe increase in muscle tone, and Grade 4 indicates a spasticty state in a flexion or extension state.

Fig. 3. (Color online) Digital hand dynamometer for measured hand grip strength.

2.4.3. Jebsen Taylor hand function test

The Jebsen Taylor hand function test was performed to evaluate the hand function of all subjects. The Jebsen Taylor hand function test contains hand function activities that are frequently used in daily life, and it is widely used in clinical practice because it can be evaluated in a short time. Measurements were made using a standardized stopwatch. A total of seven items, including writing a short sentence; flipping a card; picking up a small object; putting it into a can; mimicking eating; stacking chips; moving a large, lightweight can; and moving a large, heavy can, were measured. The time it took to execute and perform the remaining six items (except for writing the sentences) was measured. The test-retest reliability of this evaluation tool was reliable (.96–.99) [13].

2.5. Statistical analysis

A one-way ANOVA was performed to examine the differences between groups for the general characteristics of the subjects. A two-way repeated measured ANOVA was used to compare the change in dependent variables during the intervention period of brain stimulation according to the electrode placement of transcranial direct current stimulation. Interaction variables were analyzed using a one-way ANOVA measure for the amount of change, and the least square difference (LSD) was used as a posttest. SPSS statistics version 22.0 was used for the data obtained in this study, and the statistical significance level α was set to .05.

Table 1. General and medical characteristics of subjects.

	Sham-tDCS	Unilateral-tDCS	Dual-tDCS
Sex (male/female)	9/4	7/4	8/3
Etiology (Hemorrhge/Infaction)	7/6	6/5	5/6
Age	54.68 ± 7.72[a]	53.29 ± 7.94	55.87 ± 8.34
Height (cm)	166.38 ± 7.32	168.72 ± 8.47	167.76 ± 7.24
Weight (kg)	65.87 ± 8.64	66.75 ± 7.94	65.71 ± 6.92
Time onset (month)	8.38 ± 4.14	7.64 ± 4.97	8.75 ± 5.91

[a]Mean ± SD, tDCS: Transcranial Direct Current Stimulation

3. Results and Discussion

Table 1 summarizes the demographics and medical history of the subjects; there were no statistically significant differences between the three groups. The grip strength of the three groups the placebo stimulation group, the unilateral brain stimulation group, and the bilateral brain stimulation group all significantly increased ($p<.05$). A significant difference ($p<.05$) was found in the grip strength before and after treatment in between the three groups. In the post-hoc, a significant difference was found between the placebo-stimulated group and the unilateral brain stimulation group and between the placebo-stimulated group and the bilateral brain stimulated group ($p<.05$) (Table 2). The results are shown in Fig. 4. When the muscle tone changes in the elbow flexor and wrist flexor were compared before and after treatment in the three groups, there was no significant difference between the placebo stimulation group, the unilateral brain stimulation group, and bilateral brain stimulation group ($p>.05$). When the muscle tone was compared before and after treatment in the groups, there was no significant difference between the groups ($p>.05$) (Table 2). The results are shown in Figs. 5, 6. When the results of the Jebsen Taylor hand function test was compared before and after treatment in the three groups, hand function significantly decreased ($p<.05$) in the placebo stimulation group, the unilateral brain stimulation group, and bilateral brain stimulation group. A significant difference ($p<.05$) was found in the Jebsen Taylor hand function test before and after treatment in between the three groups ($p<.05$). In the post-hoc, a significant difference was found between the placebo stimulated group and the unilateral brain stimulated group ($p<.05$) (Table 2). The results are shown in Fig. 7.

In this study, for four weeks, transcranial direct current stimulation and grasping exercises were conducted to improve the performance of the upper extremity in stroke patients. Each variable was measured before, directly after, and two weeks after treatment to evaluate the effects of electrode placement on grip strength, upper extremity muscle tone, and the results of the Jebsen Taylor hand function test. The experimental groups were given tDCS in addition to the grasping motions and were divided into

Table 2. Comparison of change in variables in each group.

variables	Group	Pre	Post	Follow-up	p	F(p)		
						Group	Period	Group*Period
hand grip strength	Sham	31.73 ± 6.51[a]	35.80 ± 7.72	35.62 ± 7.05	.045*	2.87 (.072)	28.78** (.000)	2.61* (.044)
	Unilateral	32.78 ± 6.82	38.90 ± 8.31	39.36 ± 8.24	.025*			
	Dual	30.39 ± 5.69	37.74 ± 5.75	36.92 ± 5.92	.001*			
Elbow Flexor	Sham	1.92 ± 0.64	1.84 ± 0.68	1.76 ± 0.71	.224	0.63 (.542)	3.52* (.042)	0.65 (.632)
	Unilateral	1.82 ± 0.87	1.64 ± 0.80	1.55 ± 0.84	.113			
	Dual	2.09 ± 0.83	1.99 ± 0.77	1.81 ± 0.81	.157			
Wrist Flexor	Sham	2.15 ± 0.68	2.07 ± 0.64	2.07 ± 0.64	.452	1.00 (.379)	3.78* (.034)	1.35 (.263)
	Unilateral	2.09 ± 0.70	1.81 ± 0.75	1.72 ± 0.79	.124			
	Dual	2.36 ± 0.67	2.27 ± 0.75	2.08 ± 0.75	.174			
JTT	Sham	74.69 ± 11.97	71.38 ± 13.41	69.24 ± 12.17	.045*	1.20 (.314)	8.70** (.001)	2.92* (.028)
	Unilateral	77.54 ± 14.97	70.18 ± 10.89	67.24 ± 12.37	.009**			
	Dual	72.73 ± 16.22	67.54 ± 13.84	65.27 ± 10.97	.024*			

[a]Mean ± SD, *p< .05, **p< .01, Elbow Flexor: Elbow Flexor Muscle Tone, Wrist Flexor: Wrist Flexor Muscle Tone, JTT: Jebsen-Taylor hand function test

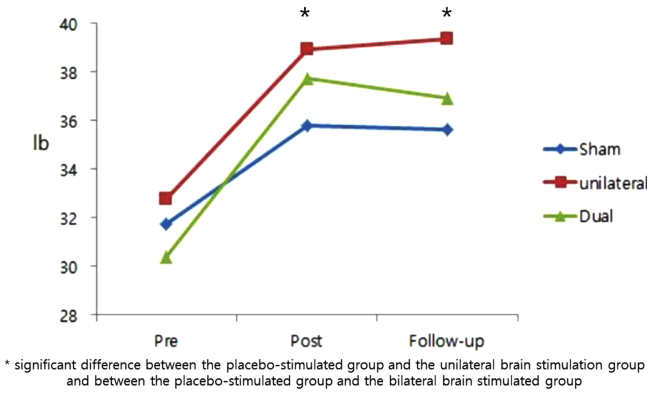


Fig. 4. (Color online) Comparison of change in hand grip strength of between the three group.

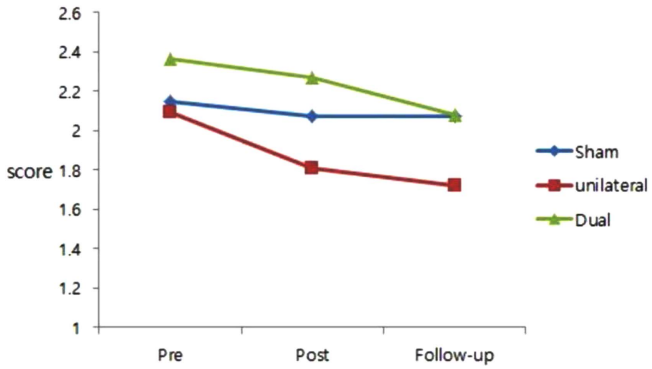


Fig. 6. (Color online) Comparison of change in wrist flexor muscle tone of between the three group.

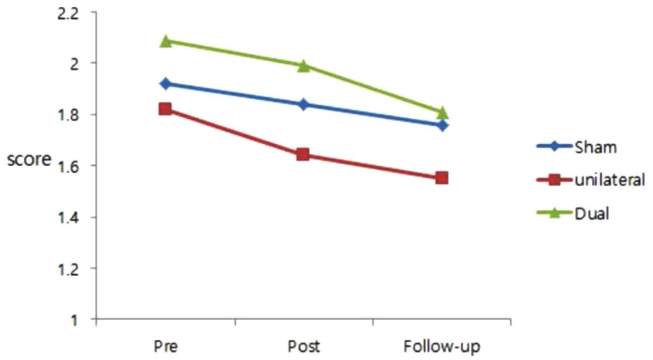


Fig. 5. (Color online) Comparison of change in elbow flexor muscle tone of between the three group.

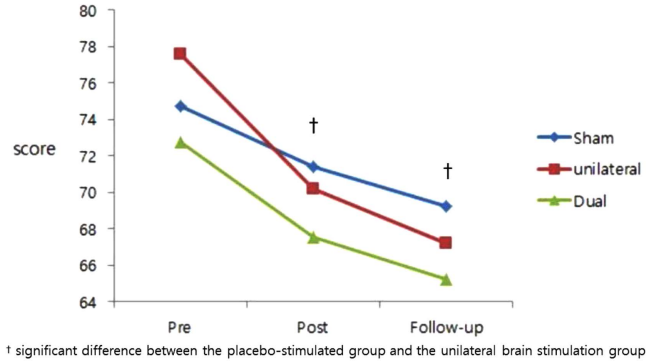


Fig. 7. (Color online) Comparison of change in JTT score of between the three group.

a unilateral brain stimulation group and a bilateral brain stimulation group, according to the electrode placement method.

In this study, the grip strength was significantly increased between the three testing periods in all groups, and the grip strength was significantly increased in the unilateral brain stimulation group and the bilateral brain stimulation group more than in the placebo-stimulated group. According to a previous study, which measured the change in the grip strength of stroke patients using bilateral brain stimulation and forced induction exercise therapy (CIMT), the group applying CIMT alone showed no significant increase in muscle strength. The group applying CIMT and tDCS together showed a significant increase in grip strength, which was consistent with the results of this study [14]. In addition, when comparing the grip training group, the tDCS group, and the group that used both grip training and direct tDCS, the exercise potential and muscle strength were significantly higher than in the other two groups. The results were increased, and the results of this study were consistent [15].

There was no significant difference between pretreatment, posttreatment, and posttest in each of the three groups, and there was no significant difference between the groups. In previous studies, tDCS applied to chronic stroke patients with mild to moderate functional limitations in the upper extremity produced a decrease in muscle tone [16]. In addition, it was reported that a ten-minute application of tDCS for five days to patients with severe chronic stroke showed a decrease in muscle tone [17]. As described above, most of the previous results showed a decrease in muscle tone after direct tDCS, but they were not consistent with the results of this study. The difference between this study and the previous ones is that the muscle strength exercise was applied simultaneously in this study, and the muscle strength exercise acted as a factor to increase muscle tone. That is my belief. Previous studies evaluating the relationship between strength training and muscle tone have suggested that strength training can increase muscle tone [18]. Therefore, in selecting training to increase muscle strength, various practice conditions must be met to solve problems with

movement and to use optimal control strategies to achieve functional proficiency.

The execution time of the Jebsen Taylor hand function test was significantly decreased in all three testing times in all groups, and the execution time was significantly decreased in the unilateral brain stimulation group more than in the placebo stimulation group. According to a previous study, Jebsen Taylor hand function test execution time was reduced as a result of stimulating tDCS in M1 in chronic stroke patients twice for ten days [19]. In addition, as a result of applying tDCS for 20 minutes to the nondominant side M1 of normal people, a significant decrease in the execution time of the Jebsen Taylor hand function test was reported, which was consistent with the results of this study. In other words, it is thought that the performance of the cortical activity increased with the application of tDCS. For example, it was confirmed that PET, rCBF, and blood flow activity increased when the positive electrode was applied to the hand region of the primary exercise area M1 and decreased when the negative electrode was applied.

The limitations of this study are as follows. First, it was difficult to generalize the results to all stroke patients. Further research is needed to investigate the effects of tDCS in specific types of stroke and with different severity levels. Second, the tDCS period was short. Further research will be needed to investigate changes in daily living performance through long-term, continuous tDCS.

4. Conclusion

To summarize the results of this study, tDCS, which can directly enhance or suppress brain activity at a specific site, can be used in conjunction with other exercises and is easy and effective in improving the function and performance of stroke patients. A clear mechanism for efficacy of the application site and the effect has not been established, and the effect of the use of the cathode is unclear. Despite these inadequacies, it is considered a therapeutic approach that can be used for a variety of purposes.

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