Original paper

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Effect of transcranial direct current stimulation combined with a smart hand joint training device on hand dysfunction in patients with early stroke

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Abstract

Introduction: *The aim of this study was to investigate the effect of transcranial direct current stimulation (tDCS) combined with a smart hand joint training device on hand dysfunction in patients with early stroke.*

Material and methods: *This study was a randomized controlled trial, which was conducted in the neurology department in our hospital. From March 2019 to January 2021, 60 patients diagnosed with early stroke hand dysfunction were selected. A random number table method was used to divide patients equally into control group (smart hand joint training device group) and intervention group (tDCS and smart hand joint training device group). Before and after treatment, Brunnstrom six-level staging, Fugl-Meyer motor function score (wrist hand part), hemiplegic finger function examination, and hemiplegic hand function classification evaluation were applied in both groups. Main outcome measures were Brunnstrom motor function staging (hand part), functional evaluation of hemiplegic fingers, and Fugl-Meyer motor function score (wrist hand part).*

Results: *After treatment, compared with control group, the results in intervention group of Brunnstrom six-level staging and hemiplegic hand function classification evaluation showed obvious improvement ($p = 0.000$), and the result of hemiplegic fingers' functional evaluation also improved ($p = 0.026$). After treatment, Fugl-Meyer motor function scores were 6.73 ±6.65 (control group) and 9.8 ±6.66 (intervention group). Slight tDCS-related adverse events occurred in one patient (3.33%) in intervention group. None in either group discontinued treatment.*

Conclusions: *Both the smart hand joint training device alone and tDCS combined with the smart hand joint training device can improve hand function of patients with early stroke to varying degrees, but the treatment effect of tDCS combined with the smart hand joint training device is more significant.*

Key words: *stroke, hand function, smart hand joint training device, transcranial direct current stimulation.*

Introduction

Stroke has become one of the main causes of disability in adults [12]. Due to complexity of the hand structure and clinicians' neglect of hand function recovery, the recovery of hand function after a stroke often lags recovery of other proximal joints. Among the surviving patients with stroke, only 5-20% fully recover their function [8], 70-80% of patients would have hand dysfunction in early stage of the disease, and 40% of them would have sequelae of hand dysfunction [22], which seriously affects their quality of life.

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Studies [25] have shown that exercise training is conducive to re-organization of the motor cortex, and re-organization of the motor cortex is related to the degree of functional recovery. Therefore, early active and highly repetitive exercise training after a stroke can greatly promote the recovery of motor function. Smart hand joint training device (a hand rehabilitation robot) has been proven to improve hand motor functioning after a stroke. It can strengthen patient's correct behavior in training [4]; it can train a knuckle alone or train multiple knuckles at the same time to increase coordination of the fingers of the affected hand. Moreover, it can improve the motor function of patient's hand while increasing the input of patient's sensory information [23].

Transcranial direct current stimulation (tDCS) is a kind of central stimulation that applies weak direct current (1 to 2 mA) through two or more electrodes placed on the scalp to regulate activity of neurons in the cerebral cortex [10]. Some studies reported that the main cause of motor dysfunction after a stroke is the imbalance of reciprocal inhibition between the cerebral hemispheres [11]. When a tDCS anode is placed in the affected hemisphere to improve excitability of the neurons at the stimulation site, or a tDCS cathode is placed in the unaffected hemisphere to reduce excitability of the neurons at the stimulation site, a new balance can be achieved between the cerebral hemispheres, thus promoting motor function after a stroke [6]. The effect of tDCS on the recovery of post-stroke dysfunction has been confirmed by numerous studies. Some research have confirmed that the upper limb function of patients with stroke can be improved by 10% to 30% after tDCS treatment [22].

However, the combined effectiveness and application period of these rehabilitation techniques still needs further investigation. In the present study, the method of combining a smart hand joint training device with tDCS was applied to patients with hand dysfunction in early stroke to observe its' effectiveness, and investigate whether it would produce a superimposed effect.

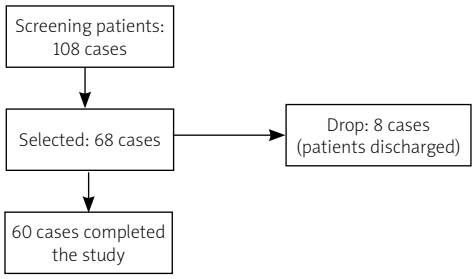

Fig. 1. Flow diagram of patients' selection.

Material and methods

Participants and experimental design

A total of 60 individuals diagnosed with ischemic stroke in the neurology department in our hospital from March 2019 to January 2021 were recruited (Fig. 1).

The inclusion criteria were as follows: 1. The diagnosis of ischemic cerebral infarction was confirmed by computed tomography or magnetic resonance imaging of the head, and the lesion was confirmed to be located on one cerebral hemisphere; 2. Brunnstrom hand staging ≥ stage II; 3. Age from 18 to 80 years; 4. Normal passive range of motion of the thumb joints, without pain or deformity; 5. First onset of early stroke within 2 weeks; 6. Informed consent provided by patients and family members.

The exclusion criteria were as follows: 1. Hemorrhage, burns, inflammation, etc., found on the skin of the hand; 2. Diagnosis of early stroke combined with comorbidities, such as severe heart, liver, kidney, or infectious diseases, head injury or tumor, and severe epilepsy; 3. Patients with implanted electronic devices (e.g., pacemakers), or metal parts in the brain or in the treatment area; 4. Sudden worsening of patient's condition; 5. Not willing to participate.

This study was a prospective, single-center, single-blinded, randomized clinical trial conducted in our city. Included patients were divided into two groups without knowing the difference in treatment according to a random number table method, and included control group (smart hand joint training device group) and intervention group (smart hand joint training device combined with tDCS group). There were 30 patients in each group, and both groups were treated with conventional treatment, including good limb position, passive limb activity, active auxiliary activity, low-frequency pulse electrical stimulation, and fastigial nucleus stimulation, once per day, 6 days per week, for 2 weeks.

Interventions

The smart joint training device protocol

All participants in both the groups received smart joint training device (Beijing Zhongjian Gaemi Technology Co., Ltd, China), and interventions were

based on conventional rehabilitation. The operation method was as follows: 1. Open all fingers; 2. The affected hand must wear a glove; 3. The electrode piece is placed on the wrist's dorsal muscle; 4. Click the interface to enter the back flexion mode; 5. Set training parameters, and click start to train hand grip, extension, and wrist back extension. The stimulation time was 20 minutes, and the treatment was carried out once per day, 6 days per week, for 2 weeks. The stimulation intensity was adjusted according to patient's tolerance. There was no statistically significant difference in the intensity of stimuli received by patients.

Transcranial direct current stimulation protocol

Intervention group used tDCS (Jiangxi Huaheng Jingxing Medical Technology Co., Ltd., China) based on conventional rehabilitation and smart joint training device intervention. The tDCS equipment included a host, a wire, two round electrodes, a fixed cap, and a charger. The operation method was as follows: 1. Soak the sponge inside the electrode sheet and install the wire; 2. Place the anode on the surface hand area of the affected hemisphere; 3. Place the cathode on the surface hand area of the unaffected hemisphere; 4. Fix the electrode with a fixed cap; 5. Turn it on and adjust the parameters; 6. It will start after resistance training (i.e., the impedance between two electrodes < 50 Ω). For the stimulation site, the anode was placed on the surface hand area of the affected hemisphere (6 cm away from the center of the apex), and the cathode was placed on the surface hand area of the unaffected hemisphere (6 cm away from the center of the apex). The stimulation time was 20 minutes, once per day. The longest treatment time was 2 weeks, and the actual treatment days were determined by the patient's hospital stay. The average treatment was 7.43 days. The stimulation intensity was 2 mA, and the patient generally had no sensation or only a slight current sensation. If the patient developed itching or tingling, the treatment was immediately stopped. After stopping treatment, these symptoms disappeared on their own.

Efficacy evaluation

Before and after treatment, both groups of patients used Brunnstrom motor function staging [12] (hand part) to evaluate gross function of the hand. Because of its' simplicity and ease of operation, it has been widely used; the Fugl-Meyer motor function score (wrist hand part) assesses functional recovery of the wrist and hand. A study of Page et al. confirmed that the wrist hand part of Fugl-Meyer assessment can be used independently, and has passed reliability and validity tests. The functional examination of hemiplegic fingers consists of 9 items, including finger group flexion, finger group extension, wrist joint separation movement, hand separation movement, speed examination, and joint reaction, which can reflect subtle changes of the hand function recovery of patients. The hemiplegic hand function classification divides the affected hand into waste hand, auxiliary hand C, auxiliary hand B, auxiliary hand A, practical hand B, and practical hand A through five actions. It is associated with daily life of patients to better judge prognosis of the affected hand.

Statistical analysis

Test results were analyzed using SPSS™ Statistics v. 21.0 software, and the measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$). If normal distribution analysis and homogeneity of variance were met, an independent sample *t* test was used for inter-group comparisons. Otherwise, a paired sample *t* test was applied for intra-group comparisons. Non-parametric test was used for non-normal distribution analysis and non-homogeneity of variance (Wilcoxon rank-sum test of two independent sample comparisons was applied for comparison between groups, and Wilcoxon signed rank-sum test of paired sample comparisons was used for comparison within groups). Test level was $\alpha = 0.05$, where $p < 0.05$ was considered statistically significant.

Results

Trial flow and baseline data

From March 2019 to January 2021, all patients in the neurology department were screened. Of these, 60 patients with hand motor impairment due to ischemic stroke were eligible for evaluation. Among these patients, none failed to meet the inclusion criteria and declined to participate in this study. All patients were assigned randomly to either the intervention group or the control group by using a table of random numbers, with 30 patients assigned to each group. No patients discontinued the intervention. Therefore, all 60 patients completed this study and

participated in the evaluations (see Flow Diagram). One patient in the intervention group reported a slight tingling sensation lasting for 3 to 5 seconds. The symptoms resolved without special treatment after stimulation was stopped, and treatment was continued thereafter.

There was no statistical difference between the two groups in general data (age, gender, lesion location, side, course of disease, and treatment time) ($p > 0.05$), indicating that the general data of the two groups were comparable before intervention. Table I demonstrates the details.

Brunnstrom motor function staging (hand part)

Before treatment, the ratings of the control group were as follows: level II: 20 cases, level III: 5 cases, level IV: 1 case, level V: 4 cases. The ratings of the intervention group were as follows: level II: 20 cases, level III: 8 cases, level IV: 2 cases. There was no statistically significant difference between the two groups before treatment ($p > 0.05$).

After treatment, the ratings of the control group were as follows: level II: 1 case, level III: 19 cases, level IV: 3 cases, level V: 1 case, level VI: 6 cases. The ratings of the intervention group were as follows: level III: 7 cases, level IV: 13 cases, level V: 10 cases. Both the groups improved significantly from their assessments before treatment ($p < 0.05$), and statistically significant improvement in the intervention group was more obvious than in the control group ($p < 0.05$). See Table II for details.

Functional evaluation of hemiplegic fingers

Before treatment, the ratings of the control group were as follows: level 2: 21 cases, level 3: 1 case, level 4: 3 cases, level 5: 1 case, level 6: 4 cases. The ratings of the intervention group were as follows: level 1: 2 cases, level 2: 21 cases, level 3: 5 cases, level 4: 2 cases. There was no statistically significant difference between the two groups before treatment ($p > 0.05$).

After treatment, the ratings of the control group were as follows: level 2: 1 case, level 3: 17 cases, level 4: 5 cases, level 6: 1 case, level 8: 2 cases, level 9: 1 case, level 10: 3 cases. The ratings of the intervention group were as follows: level 2: 2 cases, level 3:

Table I. Comparison of general data between the two groups

Group		CG (n = 30)	IG (n = 30)	P-value
Age		62.87 ±8.40	59.57 ±10.41	0.182
Gender ratio (M/F)		19/11	20/10	0.787
Course of disease (days)		7.57 ±2.75	7.67 ±2.64	0.959
Treatment duration (days)		7.33 ±1.30	7.43 ±1.25	0.762
Pathological changes, n (%)	Medulla	16 (53.33)	13 (43.33)	0.438
	Cortical	14 (46.67)	17 (56.67)	0.438
Lesion side, n (%)	Left	14 (46.67)	12 (40.00)	0.603
	Right	16 (53.33)	18 (60.00)	0.603

CG – control group, IG – intervention group, M – male, F – female

Table II. Comparison of Brunnstrom analysis between the two groups

Group	Before treatment						After treatment						Test result and p-value
Class	I	II	III	IV	V	VI	I	II	III	IV	V	VI	
CG	0	20	5	1	4	0	0	1	19	3	1	6	Z = –7.270 $p < 0.001$
IG	0	20	8	2	0	0	0	0	7	13	10	0	Z = –5.007 $p < 0.001$
Test method P-value			Z = –0.284 0.776						Z = –2.159 0.031				

CG – control group, IG – intervention group

5 cases, level 4: 11 cases, level 5: 2 cases, level 9: 5 cases, level 10: 5 cases. Both the groups improved significantly from their assessments before treatment ($p < 0.05$), and statistically significant improvement in the intervention group was more evident than in the control group ($p < 0.05$). See Table III for details.

Fugl-Meyer motor function score (wrist hand part)

Before treatment, Fugl-Meyer motor function scores of the two groups were as follows: 2.27 ±2.90 (control group) and 1.60 ±2.13 (intervention group). There was no statistically significant difference between the two groups ($p > 0.05$).

After treatment, Fugl-Meyer motor function scores of the two groups were as follows: 6.73 ±6.65 (control group) and 9.8 ±6.66 (intervention group). Both the groups improved significantly from their assessments before treatment ($p < 0.05$), and statistically significant improvement in the intervention group was more obvious than in the control group ($p < 0.05$). See Table IV for details.

Classification of hemiplegic hand function

Before treatment, the ratings of the control group were as follows: level 1: 25 cases, level 2: 1 case, level 3: 4 cases. The ratings of the intervention group were as follows: level 1: 25 cases, level 2: 5 cases. There was no statistically significant difference between the two groups before treatment ($p > 0.05$).

After treatment, the ratings of the control group were as follows: level 1: 19 cases, level 2: 4 cases, level 3: 1 case, level 4: 6 cases. The ratings of the intervention group were as follows: level 1: 7 cases, level 2: 13 cases, level 3: 2 cases, level 4: 8 cases. Both the groups improved significantly from their assessments before treatment ($p < 0.05$), and statistically significant improvement in the intervention group was more evident than in the control group ($p < 0.05$). See Table V for details.

Discussion

From the results of our study, based on conventional rehabilitation treatment, the use of a smart hand joint training device alone and smart hand joint training device combined with tDCS can both improve the hand function of patients with early stroke, and the effect of smart joint training device combined with tDCS closed-loop rehabilitation training is better than the use of smart joint training device alone.

In this study, the central-peripheral-central closed-loop rehabilitation intervention mode was used as the basic concept [8], which was to stimulate and activate the brain area through central intervention to improve neuro-plasticity. At the same time, to perform peripheral stimulation to strengthen motor control training, and form positive feedback and input to the center; thereby, promoting the re-modelling of brain function. Through the effective combination of central intervention and peripheral stimulation, a closed-loop mode of information feedback is formed, which ultimately acts on the patient's specific brain area or functionally related to brain area, thereby promoting the recovery of hand function after a stroke.

Treatment with tDCS is used as a central intervention to regulate neuronal activity in the cerebral cortex. It mainly works by applying a weak direct

Table III. Comparison of functional evaluation of hemiplegic fingers between the two groups

Group	Class	CG	IG	Test result and *p*-value
Before treatment	0	0	0	$Z = -1.370$ $p = 0.171$
	1	0	2	
	2	21	21	
	3	1	5	
	4	3	2	
	5	1	0	
	6	4	0	
	7-12	0	0	
After treatment	0	0	0	$Z = -2.225$ $p = 0.026$
	1	0	0	
	2	1	2	
	3	17	5	
	4	5	11	
	5	0	2	
	6	1	0	
	7	0	0	
	8	2	0	
	9	1	5	
	10	3	5	
	11	0	0	
	12	0	0	
Test method *P*-value		$Z = -4.777$ ≤ 0.001	$Z = -4.385$ ≤ 0.001	

CG – control group, IG – intervention group

Table IV. Comparison of Fugl-Meyer motor function score (wrist hand part) between the two groups

Group	Before treatment	After treatment	Test result and *p*-value
CG	2.27 ±2.90	6.73 ±6.65	Z = –4.842 *p* < 0.001
IG	1.60 ±2.13	9.8 ±6.66	Z = –4.793 *p* < 0.001
Test method *P*-value	Z = –0.599 0.549	Z = –2.493 0.013	

CG – control group; IG – intervention group

Table V. Comparison of functional classification of hemiplegic hand between the two groups

Group	Before treatment						After treatment						Test result and *p*-value
Class	0	1	2	3	4	5	0	1	2	3	4	5	
CG	0	25	1	4	0	0	0	19	4	1	6	0	Z = –3.006 *p* < 0.001
IG	0	25	5	0	0	0	0	7	13	2	8	0	Z = –4.304 *p* < 0.001
Test method *P*-value	Z = –0.228 0.820						Z = –2.399 0.016						

CG – control group; IG – intervention group

current (e.g., 1-2 mA) [10] with two or more electrodes placed on the scalp. The anode is placed in the affected hemisphere to improve the excitability of neurons at the stimulation site, or the cathode is placed in the unaffected hemisphere to reduce the excitability of neurons at the stimulation site, so that a new balance can be achieved between the cerebral hemispheres [6]. The treatment with tDCS can also increase synaptic plasticity by inducing the release of neuro-transmitters [20], stimulate the primary motor center of the cerebral hemisphere to increase the excitability of the cortex [15], regulate regional cerebral blood flow, save ischemic penumbra reversible brain tissue, and promote the recovery of damaged function [24]. Moreover, it also has a remote post-synaptic effect [13].

In recent years, many scholars have conducted research on the effectiveness of tDCS on hand motor dysfunction after a stroke. Allman [1], Jia [8], Fan [5], Wu [22], and Zhu *et al*. [25] used an anode to stimulate affected hemisphere; while Rabadi [17], Au-Yeung [2], and Fusco *et al*. [7] used a cathode to stimulate unaffected hemisphere. The results showed that both the anode stimulation and cathode stimulation were effective in the treatment of hand dysfunction. Some studies also reported using tDCS bilateral stimulation (anode stimulation of affected hemisphere and cathode stimulation of unaffected hemisphere), such as Lefebvre [9], Salazar [18], Chen *et al*. [4], which also confirmed the effectiveness of tDCS. Vines [21] found that bilateral tDCS can better correct the imbalance between the cerebral hemispheres, increase the synchronization of patients' brain's local activities, and be more conducive to the recovery of motor function of patients with stroke. However, these scholars mainly focused on research in sub-acute and chronic phases. There are very few applications of tDCS bilateral stimulation in the acute phase. Therefore, our research mainly applied tDCS bilateral stimulation to the acute phase of stroke and observed its' effectiveness. Therefore, in this study, the patients were treated about 7 days after onset, and the results showed that after an average of 7 days (range, 4-10 days) of treatment, good results were also achieved.

Compared with other central interventions [16], the advantages of tDCS include its' portability, no damage, low cost, safety, and long-lasting effect. The common adverse reactions are itching and tingling, but they generally last for a short time and are not severe. These symptoms can disappear on their own after treatment is stopped, and there is no need to deal with them separately. In the present study, one patient felt a slight tingling pain, and the symptoms disappeared after adjusting the electrode pads. No other patient experienced adverse reaction.

The smart hand joint training device is selected as a passive peripheral intervention measure. It is also called a flexible hand-functional rehabilitation robot, which uses pneumatic power to automatically drive passive activities, such as finger grasping, gripping, and stretching. Relevant studies have shown that passive activities in early stages of stroke can also activate relevant brain areas, promote brain function re-organization and are more conducive to the rehabilitation of patients [23]. Moreover, the smart hand joint training device can provide repetitive, timed, quantitative, and gradual rehabilitation treatment for patients with stroke, reduce the burden on medical staff, increase patient's chances of obtaining rehabilitation, and ensure the intensity of rehabilitation training [10]. At the same time, the smart joint training device can also strengthen patient's correct behavior in training [4], including grasping ability, to better employ the abilities learned in training to real life. This reduces the process of converting grasping ability in rehabilitation training into daily life skills and shortens the process of training, which is more conducive to patient recovery.

A study [23] have shown that the synchronization of sensory and motor information in sports training assisted by smart joint training devices is better than traditional rehabilitation synchronization. This is more helpful for patient to form the correct sensory-motor circuit as well as for the re-modelling of nerve function, and is more conducive to patient's recovery. Sale *et al*. [19] used hand rehabilitation robots in clinical practice for the first time and proved their effectiveness. Subsequently, Orihuela-Espina [14], Calabro [3], and Xiao *et al*. [23] conducted related studies, all of which confirmed that the hand rehabilitation robot can promote the recovery of patient's hand motor function.

In the present study, the smart joint training device combined with tDCS was applied in the acute stage of stroke, forming a central-peripheral-central closed-loop rehabilitation mode. It acts on the patient's hand area to better promote the recovery of hand function after a stroke.

However, this study still has many shortcomings: 1. We adopted four evaluation methods, but there were subtle functional improvements that could not be reflected in the evaluation scales; 2. In the application of tDCS, many influencing factors (intervention period, stimulation site, stimulation intensity, stimulation time, severity of the patient's condition, course of disease, gender, etc.) affected treatment outcome. Therefore, in future research, we should conduct in-depth discussions on unified standards, standardized treatment, and objective evaluation. At the same time, attention should be paid to follow-up of patients in further study.

Conclusions

Based on conventional rehabilitation treatment, the use of a smart hand joint training device alone and a smart hand joint training device combined with tDCS can both improve the hand function of patients with early stroke, and the effect of closed-loop rehabilitation training of a smart hand joint training device combined with tDCS is better than the use of a smart joint training device alone.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. This study was conducted with approval from the ethics committee of The Second Hospital of Hebei Medical University (No.: 2019-R086). Written informed consent was obtained from all participants.

Disclosure

The authors report no conflict of interest.

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