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Original Article

Effect of combination of transcranial direct current stimulation and feedback training on visuospatial neglect in patients with subacute stroke: a pilot randomized controlled trial

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Abstract. [Purpose] To investigate the effects of a combination of transcranial direct current stimulation (tDCS) and feedback training (FT) on subacute stroke patients with unilateral visuospatial neglect. [Subjects] The subjects were randomly assigned to a tDCS + FT group (n=6) and a FT group (n=6). [Methods] Patients in the tDCS + FT group received tDCS for 20 minutes and then received FT for 30 minutes a day, 5 days a week for 3 weeks. The control group received FT for 30 minutes a day, 5 days a week for 3 weeks. [Results] After the intervention, both groups showed significant improvements in the Motor-Free Visual Perception Test (MVPT), line bisection test (LBT), and modified Barthel index (MBI) over the baseline results. The comparison of the two groups after the intervention revealed that the rDCS + FT group showed more significant improvements in MVPT, LBT, and MBI. [Conclusion] The results of this study suggest that tDCS combined with FT has a positive effect on unilateral visuospatial neglect in patients with subacute stroke.
Key words: TDCS, Feedback training, Neglect

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INTRODUCTION

Unilateral visuospatial neglect is a neurological disorder that occurs frequently after stroke. It is defined as the loss of visual perception of objects within the visual area opposite to the lesion hemisphere[1, 2)]. Unilateral visuospatial neglect aggravates the recovery of functional ability[3)], and delays the motor recovery phase of stroke patients[4)]. Thus, many therapeutic approaches that aim to reduce the symptoms of visuospatial neglect in stroke patients have been investigated (e.g. visual scanning training, limb activation, mental imagery, feedback training, sensory stimulations, and prism adaptation)[5)]. However, there is a dearth of guidance on the choice of the approach method[6)].

Feedback training (FT) was recommended for the rehabilition of patients with visuospatial neglect in a systematic review by Luauté et al[5)]. FT requires subjects to look at the center of a mirror so that they can see the reflection of the body on the side of visuospatial neglect. The FT approach is reported to have a positive effect in cases who lack appropriate awareness of a neurological deficit who are recognized as having poor treatment outcome[5)].

Transcranial direct current stimulation (tDCS) activates a specific area of the brain non-invasively, and can induce polarity-specific excitability changes in the brain[7, 8)]. Recently, tDCS has gained increasing attention as a the treatment method for visuospatial neglect[7)]. The area of the right posterior parietal cortex has been suggested that to be a suitable target area for improving motor functions and alleviating the symptoms of visuospatial neglect[7)]. tDCS increases cortical excitability and changes the neural structures in damaged areas of the brain, inducing neuroplasticity[9, 10)].

Several studies[7, 11)] have reported the benefical effect of tDCS for visuospatial neglect patients. However, to our knowledge, no study has investigated combined methods (tDCS + FT), using randomized controlled trials, and compared the effect of tDCS on visuospatial neglect in patients with acute stroke. Therefore, this study was performed to investigate the effects of tDCS combined with FT in subcute stroke patients with unilateral visuospatial neglect.

SUBJECTS AND METHODS

The subjects were selected from among those with unilateral visuospatial neglect admitted to W university hospital in the Republic of Korea. They were randomly divided into two groups. Subjects who provided their informed consent and met the inclusion criteria were enrolled in this study.

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The inclusion criterion was more than 15% deviation to the right from the center in the line bisection test (LBT)[12]. The exclusion criteria were (1) severe cognitive impairment rendering a person unable to understand the instructions given by a therapist; (2) contraindications for intervention; or (3) unstable medical or neurologic conditions.

Participation in the study was voluntary, and the subjects fully understood the contents of this study. Written informed consent, after providing an explanation of the study purpose and the experimental method and processes, was obtained from all of the subjects. The study was approved by the institutional review board of Daejeon University and followed the principles outlined in the Declaration of Helsinki.

A three-week training study was designed to evaluate the effect of tDCS + FT on unilateral visuospatial neglect. The severity of visuospatial neglect was assessed pre- and post-treatment using the Motor-Free Visual Perception Test (MVPT) and the line bisection test (LBT). The capacity to perform daily living activities was assessed using the modified Barthel index (MBI).

The experiment began on the day after the subjects had been divided into groups. For both groups, the intervention progressed during the regularly scheduled therapy sessions and all other routine interdisciplinary stroke rehabilitation proceeded as usual. Each participant performed a training program consisting of 15 sessions lasting 50 min/day, 5 days a week for three weeks.

Subjects in the tDCS + FT group received tDCS for 20 minutes and then performed the FT training. Subjects sat on a chair with both arms on the armrest in a comfortable position. A sponge electrode of 7×5 cm^2 (area; 24 cm^2) for tDCS (Phoresor Auto model PM 700, IOMED, Salt Lake City, USA) was soaked in 0.9% physiological saline and applied to the head of the participant using as tight a band as possible without creating discomfort. The anode electrode was attached to the right posterior parietal cortex (P4) was accompanied by cathode tDCS of the second circuit was positioned over the left posterior parietal cortex (P3). Therefore, in the first tDCS circuit, the anode was placed over P4 and the cathode was placed over the left supraorbital area. Stimulation was applied with a 1 mA stimulus intensity for 20 min[7].

Both group received FT for 30 minutes a day, 5 times a week for 3 weeks. FT used a vertical mirror held parallel to the sagittal plane to provide visual feedback of participants' neglected side body. The subjects were asked to look at the center of the mirror so they could see the reflection of visual input coming from the left side of the body.

The Motor-Free Visual Perception Test (MVPT)[13] is a 36-item multiple-choice test that evaluates visuospatial neglect. The line bisection test (LBT)[14] was used to investigate the quality and severity of visuospatial neglect. The distance from the left of each line to patients' marks and to true line centers were measured. The deviation was measured. The modified Barthel index (MBI)[15] was used to evaluate activities of daily living (ADL).

Descriptive statistics were used to summarize baseline data. Category variables (gender, side of stroke) were compared between the groups using of the Fisher's exact test. Between-group comparisons of baseline characteristics (age, weight, height, time after stroke, MVPT, LBT, and MBI) were performed using the Mann-Whitney U-test. Within-group comparisons of pre- and post-test values in each group were made using Wilcoxon signed rank test and between-group comparison for post-test values were performed using the Mann-Whitney U-test. The significance level used was $p<0.05$.

Table 1. General characteristics of the subjects

	tDCS + FT group (n=6)	FT group (n=6)
Gender		
Male/Female	2/4	2/4
Paretic side		
Right/Left	0/6	0/6
Age (years)	66.0 ± 4.2	65.6 ± 4.7
Weight (kg)	67.4 ± 5.2	66.8 ± 4.9
Height (cm)	164.5 ± 7.2	164.7 ± 3.4
Duration (week)	6.5 ± 1.6	6.8 ± 1.4

*Mean±SD

tDCS: transcranial direct current stimulation; FT: feedback training

RESULTS

Participants in the tDCS + FT group performed the FT after receiving tDCS and those in the FT group performed FT without receiving tDCS. All the participants completed the entire study. There were no significant group differences in sex, side or type of stroke, time after stroke, age, MMSE (Table 1) or MVPT, LBT, or MBI score before the intervention. After the intervention, both groups showed significant differences compared with before the intervention in MVPT, LBT, and MBI ($p<0.05$). There were significant differences after intervention in the MVPT ($z=-2.75$, $p=0.006$), LBT ($z=-2.17$, $p=0.031$), and MBI ($z= -2.90$, $p=0.004$) between the two groups (Table 2).

DISCUSSION

This study was performed to evaluate the therapeutic effect of tDCS combined with feedback training (FT) in patients with subacute stroke and unilateral visuospatial neglect. Both groups showed significant changes after the intervention, and the tDCS + FT group showed more significant changes than the control group in the MVPT, LBT, and MBI results. The findings of this study show that tDCS combined with FT decreased the symptoms of visuospatial neglect significantly more than FT alone.

In recent years, brain activation has been employed in rehabilitation of brain damage[16, 17]. In the present study, tDCS was applied to the posterior parietal cortex (P4), which is the most critical lesion site for visuospatial neglect[4, 10]. The results prove that tDCS can alleviate the symptoms of visuospatial neglect.

The neural mechanism of tDCS is proposed to activate the brain leading to brain plasticity, and is potentially medi-

Table 2. Outcome measures

	tDCS + FT group (n=6)		FT group (n=6)	
	Pretest	Posttest	Pretest	Posttest
MVPT	17.3 ± 1.5[a]	30.83 ± 2.3*+	18.1 ± 1.9	25.3 ± 2.4*
LBT	11.3 ± 1.0	5.37 ± 0.4*+	10.3 ± 1.0	5.9 ± 0.3*
MBI	51.3 ± 4.8	78.3 ± 3.9*+	50. 2 ± 5.6	69.2 ± 2.4*

[a]Means ± SD
*Significant difference within group. +Significant difference between groups.
tDCS: transcranial direct current stimulation; FT: feedback training; MVPT: motor-free perception test; LBT: line bisection test; MBI: modified Barthel index
The pretest was performed before the intervention, and the posttest was performed after 3 weeks.
The significance of differences was accepted for values of $p < 0.05$.

ated by glutamatergic and neurotrophic mechanisms, which are known found to be important in activity dependent brain plasticity[1, 7, 18]. Stimulation of the posterior parietal cortex may facilitate the functioning of this brain region, and therefore improve spatial perception or awareness of the body.

The FT method is recommended with a grade B. It uses a visual-feedback procedure to increase self-awareness of the subjects visual neglect symptoms[5]. Neglect is a reduction in body awareness, response ability, or reaction to novel stimuli which can affect perception and mental representation of spatial information, as well as planning and execution of motor action[6]. Thus, overcoming visuospatial neglect is critical for the improvement of functional outcomes, both as an independent measure and in connection with other variables[19].

Applying tDCS had a positive effect on the symptoms of visuospatial neglect in subacute stoke patients in addition to the FT effect. FT has already been shown to reduce visuospatial neglect, and selective stimulation of the brain helps to improve awareness of the body[5].

This study has some limitations. First, only a small number of hospital patients in the hospital were recruited, so the data may not be representative of stroke patients as a whole. Second, there was no follow up to measure the long-term effect, so the durability of the effect could not be determined. Thus, the results should be considered with caution.

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