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ORIGINAL ARTICLE

Combination Transcranial Direct Current Stimulation and Virtual Reality Therapy for Upper Extremity Training in Patients With Subacute Stroke

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Abstract

Objective: To investigate the effects of combination cathodal transcranial direct current stimulation (tDCS) and virtual reality (VR) therapy for upper extremity (UE) training in patients with subacute stroke.

Design: Pilot randomized controlled trial. Patients were randomly assigned to 1 of 3 groups: group A received cathodal tDCS, group B received VR, and group C received combination therapy (cathodal tDCS was simultaneously applied during VR therapy).

Setting: University hospital.

Participants: Patients (N=59) with impaired unilateral UE motor function after stroke.

Intervention: Fifteen sessions of treatment over a 3-week period.

Main Outcome Measures: The Modified Ashworth Scale, manual muscle test (MMT), Manual Function Test (MFT), Fugl-Meyer Scale (FMS), and Box and Block Test were used to assess UE function. To evaluate activities of daily living, the Korean-Modified Barthel Index (K-MBI) was used. All outcomes were measured before and immediately after treatment.

Results: After treatment, all groups demonstrated significant improvements in MMT, MFT, FMS, and K-MBI scores. The change in MFT and FMS scores was different between the 3 groups. Post hoc analysis revealed that the improvement of MFT and FMS scores in group C was significantly higher than those of the other 2 groups.

Conclusions: In the present pilot study, the combination of brain stimulation using tDCS and peripheral arm training using VR could facilitate a stronger beneficial effect on UE impairment than using each intervention alone. This combination therapy might be a helpful method to enhance recovery of the paretic UE in patients with stroke.

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Impairment of upper extremity (UE) function is common in patients with stroke, and continued motor impairment of the UE restricts activities of daily living in many cases.[1-3] Current stroke rehabilitation guidelines used in clinical practice are based on increasing scientific and clinical evidence of a remarkable potential for brain remodeling because of neuroplasticity.[4,5] Several therapeutic modalities have been developed to enhance the neuroplasticity in brain representations of UE muscles after stroke.

Transcranial direct current stimulation (tDCS) alters cortical excitability by influencing N-methyl-D-aspartate and gamma-aminobutyric acid receptors.[6-8] The effect of anodal tDCS is to upregulate the excitability of the ipsilesional primary motor cortex; however, the effect of cathodal tDCS is to downregulate the excitability of the unaffected motor cortex.[9,10] tDCS produces fewer artifacts than transcranial magnetic stimulation, such as acoustic noise and muscle twitching, and it is inexpensive. In addition, no seizure incidents have been reported.[11,12] Cathodal tDCS may have use as an adjuvant therapy for the UE function after stroke.[13-15] Cathodal tDCS improved selective UE control for mildly impaired patients compared with moderate to severely impaired patients.[16] Some studies have reported that cathodal

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stimulation demonstrates more improvements in UE function than anodal or sham stimulation.[15,17]

Virtual reality (VR) is computer-based technology that allows users to interact with a multisensory simulated environment and receive real-time feedback on performance. VR exercise applications have the potential to apply relevant concepts of neuroplasticity.[3,18-21]

Several combination trials have been performed on these new therapeutic modalities. Celnik et al[22] suggested that combination anodal tDCS and peripheral nerve stimulation could facilitate the beneficial effects in comparison with each intervention alone. Another combination therapy that incorporated tDCS and robot-assisted arm training for the rehabilitation of patients with subacute stroke was conducted.[17] In that study, 3 different types of tDCS were applied (anodal, cathodal, and sham stimulation), but no significant changes between groups were noted.

To our knowledge, no study has yet evaluated a combination therapy using tDCS and VR. Brain stimulation using tDCS, in combination with a VR program to facilitate UE movements, could represent a viable new treatment option. The aim of this study is to investigate the effect of combined cathodal tDCS and VR therapy on UE training in patients with subacute stroke. We hypothesized that cathodal tDCS would suppress contralesional hyperexcitability because this activation is prominent in the subacute stroke stage.[23-25] VR would presumably modulate cortical reorganization.[20]

Methods

Participants

This pilot randomized controlled trial was performed in the Department of Rehabilitation at Asan Medical Center, Seoul, Republic of Korea. Patients who were admitted or transferred to our department because of unilateral hemiparesis caused by stroke were evaluated. All of the included patients had had their first stroke within 1 month prior to enrollment, and their motor power of the affected shoulder was considered greater than a poor grade (ie, patients could not perform movements against gravity, but they demonstrated complete range of motion when the pull of gravity was eliminated). Exclusion criteria included patients with contraindications to brain stimulation, previous history of brain neurosurgery or epilepsy, or metallic implants in the brain. Patients who had severe cognitive impairments or aphasia, which made them unable to understand the instructions given by therapists, were excluded. Patients who could not complete the VR protocol because of poor sitting balance, severely damaged eyesight, or hemispatial neglect were also excluded.

Interventions

All of the enrolled patients were randomly assigned to 1 of 3 groups using a table of random numbers; group A received cathodal tDCS during occupational therapy, group B received VR instead of occupational therapy, and group C received combination cathodal tDCS and VR therapy. In group C, cathodal tDCS was simultaneously applied during VR therapy. Each training protocol was applied over 15 sessions (30min/d and 5 times/wk for 3wk). For the duration of the study, all subjects received conventional rehabilitation, including physical, occupational, and cognitive therapies, of the same intensity and time. Therapists were blinded to the study design. A single therapist who was blind to group allocation conducted the VR therapy in groups B and C.

tDCS was delivered using a Phoresor II Auto Model PM850[a] via 2 conductive rubber electrodes that were placed in saline-soaked sponges ($5.0 \times 5.0 cm^2$) (fig 1). The cathodal electrode was placed over the hand area of the unaffected motor cortex, whereas the anodal electrode was placed above the contralateral orbit of the eye. To determine the optimal cortical stimulation site representing the hand area, we recorded the motor evoked potential in the unaffected first dorsal interossei muscles using transcranial magnetic stimulation.[b] The stimulation site was the site where the lowest excitatory threshold, shortest latency, and largest average amplitude in the resting state were recorded. The tDCS intensity was 2mA, and the duration of the stimulation application was 20 minutes.

VR (fig 2A) was performed using a VR system[c] that consisted of a monitor, video camera, and computer that recognized the system's gloves and virtual objects. The video camera recognizes the movements and/or position of the patient and transfers him or her into the virtual space. The computer gloves read the responses of the patient and transfers it to the VR system. The patient was able to view their own body movements in real time, which allowed the patient to be immersed inside the virtual environment. The VR training protocol consisted of the 3 following programs: (1) bird and ball, in which the patient touches a flying ball with their hand, which then turns it into a bird (fig 2B); (2) conveyor, in which the patient moves a box to a container on the opposite side (fig 2C); and (3) juggler, in which the patient catches a ball and tosses it up again (fig 2D). In these programs, patients were told to use the affected arm; when patients could not respond to the stimuli, the therapist encouraged and helped them to respond. The glove was applied only to the paretic arm (see fig 2).

List of abbreviations:

FMS	**Fugl-Meyer Scale**
K-MBI	**Korean-Modified Barthel Index**
MFT	**Manual Function Test**
MMT	**manual muscle test**
tDCS	**transcranial direct current stimulation**
UE	**upper extremity**
VR	**virtual reality**

Fig 1 tDCS was administered using Phoresor II Auto Model PM850 via 2 conductive rubber electrodes that were placed in saline-soaked sponges.