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Enhancement of Cortical Excitability and Lower Limb Motor Function in Patients With Stroke by Transcranial Direct Current Stimulation

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ABSTRACT

Background: Motor dysfunction in the lower limbs is a common sequela in stroke patients.
Objective: We used transcranial magnetic stimulation (TMS) to determine if applying transcranial direct current stimulation (tDCS) to the primary motor cortex helps enhance cortical excitability. Furthermore, we evaluate if combination anodal tDCS and conventional physical therapy improves motor function in the lower limbs.
Methods: Twenty-four patients with early-stage stroke were randomly assigned to 2 groups: 1) the tDCS group, in which patients received 10 sessions of anodal tDCS and conventional physical therapy; and 2) the sham group, in which patients received 10 sessions of sham stimulation and conventional physical therapy. One day before and after intervention, the motor-evoked potential (MEP) of the affected tibialis anterior muscle was evaluated and motor function was assessed using the lower limb subscale of the Fugl-Meyer Assessment (FMA-LE), lower limb Motricity Index (MI-LE), Functional Ambulatory Category (FAC), Berg Balance Scale (BBS), and gait analysis.
Results: The MEPs in the tDCS group became shorter in latency and higher in amplitude after intervention in comparison with the sham group. Improvements in FMA-LE and MI-LE were greater in the tDCS group, but no significant differences in FAC or BBS scores were found. Also, the changes observed on the gait analyses did not significantly differ between the tDCS and sham groups.
Conclusion: Combination anodal tDCS and conservative physical therapy appears to be a beneficial therapeutic modality for improving motor function in the lower limbs in patients with subacute stroke.

Introduction

Stroke can cause many types of neurological deficits [1]. Motor dysfunction in the lower limbs is one of the most common disabling sequela that affects stroke patients [2]. Conventional physical therapy is applied to rehabilitate most patients with motor dysfunction, including neurodevelopment techniques and task-oriented gait training [3]. Recently, invasive and noninvasive neurostimulation approaches have been developed to modulate the human brain [4–7]. These neurostimulations influence cortical excitability in the brain [8,9] and enhance motor function in stroke patients [10–15]. Therefore, along with conventional rehabilitation, many clinicians have applied various forms of neurostimulation to treat motor dysfunction.

Several invasive and noninvasive neurostimulation studies have attempted to modulate cortical excitability in the human brain. Enhanced cortical excitability could induce functional improvements in stroke patients [16–21]. Transcranial direct current stimulation (tDCS) is one recently described noninvasive technique. tDCS continuously applies a low-intensity electrical current between 2 electrodes placed over the scalp [22,23]. Anodal stimulation increases cortical excitability, whereas cathodal stimulation

Abbreviations: ANCOVA, one-way analysis of covariance; BBS, Berg Balance Scale; CST, corticospinal tract; ET, excitatory threshold; FAC, Functional Ambulatory Category; FMA-LE, Fugl-Meyer Assessment; MEP, motor-evoked potential; MI-LE, lower extremity Motricity Index; TA, tibialis anterior; tDCS, transcranial direct current stimulation; TMS, transcranial magnetic stimulation.

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decreases it. Functional neuroimaging and transcranial magnetic stimulation (TMS) studies report that tDCS can modulate motor cortex excitability in normal patients [16,18,19]. However, little is known about this topic in stroke patients, and knowledge regarding the mechanisms of motor recovery following tDCS remains limited in stroke patients.

In our current TMS study, we report enhanced cortical excitability after applying anodal tDCS over the lower limb primary motor cortex in patients with subacute stroke. We also investigated if this altered excitability is related to improvements in lower limb motor function.

Patients and methods

Patients

We prospectively recruited 24 consecutive stroke patients who were admitted to the Department of Physical Medicine and Rehabilitation at a University Hospital. All patients provided signed informed consent, and the study protocol was approved by the institutional review board of Asan Medical Center. The inclusion criteria included the following: (1) first unilateral ischemic stroke in the cortical or subcortical area; (2) stroke diagnosed within 7–30 days of a cerebral infarct onset; (3) hemiparesis at the time of evaluation; (4) age between 21 and 80 years; and (5) walking without physical assistance. Exclusion criteria included the following: (1) severe somatosensory, apraxia, or cognitive impairments; (2) serious medical complications, such as pneumonia or cardiac problems, from onset to final evaluation; and (3) lesions in the cerebellum or brain stem.

Experimental design

This study was designed and performed as a prospective, randomized, controlled clinical trial. All patients were randomly assigned to 2 groups: 12 patients in the tDCS group and 12 patients in the sham group. Depending on the assigned group, patients underwent 2 different stimulations: either anodal tDCS or sham stimulation to the affected hemisphere. Both anodal tDCS and the sham stimulations were delivered through 2 saline-soaked sponge surface electrodes using a battery-driven constant current stimulator (Phoresor II Auto; Iomed, Inc., Salt Lake City, UT). Stimulations were delivered while the patient was receiving conventional physical therapy. All patients also received movement therapy for 6 days/week (Monday–Friday: 2.5 h/day; Saturday: 1 h/day), which was primarily administered to improve postural control, motor function, and movement patterns in the affected extremities. The center of the anodal electrode was placed above the tibialis anterior (TA) area of the precentral gyrus in the affected hemisphere. To confirm the exact location of this area, the optimal scalp site for the affected cortex was determined using TMS. TMS was performed using a Magstim 200 stimulator (Magstim Co., Dyfed, UK) with a 9-cm circular coil. A cloth marked with a 1 cm × 1 cm grid and Cz-referenced to the intersection of the midsagittal and interaural lines was placed on the scalp.

The excitatory threshold (ET) was defined as the minimum stimulus required to elicit a motor-evoked potential (MEP) with a ≥50 μV peak-to-peak amplitude in 2 of 4 attempts. The stimulation intensity was set to ET plus 20% when the ET was <80%, or at 100% of the stimulator output when the ET was >80%. In all patients, magnetic stimulation was applied at 100% of the maximum output. MEPs were obtained from the hemiparetic TA muscle. Each site was stimulated 4 times at 1-cm intervals with a minimum of 10 s between stimulations, and the location that demonstrated the shortest latency and largest peak-to-peak amplitude was chosen as the optimal scalp site. We obtained MEPs from the hemiparetic TA muscle in all evaluated patients. The cathode electrode was then placed on the forehead above the contralateral supraorbital area, and the current was run through the brain and other tissues of the head from the anodal to cathodal electrode. The diameter of the anodal electrode was 3 cm (7.07 cm^2), and that of the cathodal electrode was 6 cm (28.26 cm^2). We used the small anodal electrode to give focal stimulation to underlying cortex.

In the tDCS group (conventional therapy + anodal tDCS), the current was delivered for 10 min at 2 mA, which has been proven as safe by prior studies. The same procedure was used for the sham group, but the current was only delivered for the initial 15 s. For the sham group (conventional therapy + sham stimulation), the electrodes were maintained so that no participants knew which stimulation they were receiving. Anodal tDCS or sham stimulation was administered once-daily for 2 weeks (Monday–Friday for a total of 10 sessions) to each group (Fig. 1). The experimenters who applied the anodal tDCS or sham stimulations were different from the experimenters who measured the outcomes. The experimenters who determined the results of the MEP data and those who measured physical function were blind to each other's results. The experiments for assessing MEP were blind to patient information, such as the group assignment and the outcomes of any functional evaluations. Also, the therapists who performed conventional therapy were blind to the group assignment. After completing each stimulation session, the experimenter who applied the interventions asked the patient if they could differentiate the interventions they had received.

MEP and functional evaluation

The MEP results of the TA and gait analyses, as well as the lower limb subscale of the Fugl-Meyer Assessment (FMA-LE) [24], lower limb Motricity Index (MI-LE) [25], Functional Ambulatory Category (FAC) [26], and Berg Balance Scale (BBS scores) [27], were used to evaluate motor function in the lower limb on the day before the tDCS or sham stimulations were administered (Pre) and 1 day (approximately 24 h) after administering the 10 stimulations (Post) (Fig. 1).

MEPs were measured from the site where the center of the anodal tDCS electrode was placed. The site was stimulated 4 times at 10-s intervals, and the MEPs with the shortest latency and largest

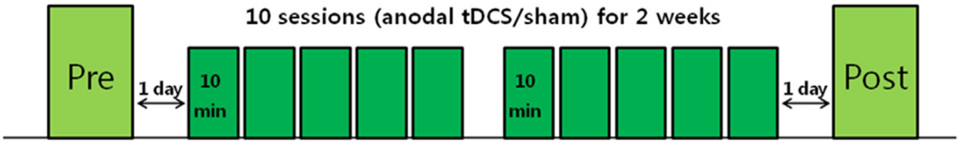

Figure 1. Experimental design. Motor-evoked potential in the tibialis anterior, the lower limb subscale of the Fugl-Meyer Assessment, lower limb Motricity Index, Functional Ambulatory Category, Berg Balance Scale scores, and the results of gait analyses were assessed at baseline (Pre) and 1 day after intervention (Post). Patients were randomly assigned to receive anodal transcranial stimulation or sham stimulation. Ten sessions (five 10-min sessions/week for 2 weeks) of anodal transcranial direct current stimulation or sham stimulation were applied during conventional physical therapy.