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Original article

Effect of single-session dual-tDCS before physical therapy on lower-limb performance in sub-acute stroke patients: A randomized sham-controlled crossover study

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ABSTRACT

Anodal stimulation increases cortical excitably, whereas cathodal stimulation decreases cortical excitability. Dual transcranial direct current stimulation (tDCS; anodal over the lesioned hemisphere, cathodal over the non-lesioned hemisphere) was found to enhance motor learning. The corresponding tDCS-induced changes were reported to reduce the inhibition exerted by the unaffected hemisphere on the affected hemisphere and restore the normal balance of the interhemispheric inhibition. Most studies were devoted to the possible modification of upper-limb motor function after tDCS; however, almost no study has demonstrated its effects on lower-limb function and gait, which are also commonly disordered in stroke patients with motor deficits. In this randomized sham-controlled crossover study, we included 19 patients with sub-acute stroke. Participants were randomly allocated to receive real or sham dual-tDCS followed by conventional physical therapy with an intervention interval of at least 1 week. Dual-tDCS was applied over the lower-limb M1 at 2-mA intensity for 20 min. Lower-limb performance was assessed by the Timed Up and Go (TUG) and Five-Times-Sit-To-Stand (FTSTS) tests and muscle strength was assessed by peak knee torque of extension. We found a significant increase in time to perform the FTSST for the real group, with improvements significantly greater than for the sham group; the TUG score was significantly increased but not higher than for the sham group. An after-effect on FTSTS was found at approximately 1 week after the real intervention. Muscle strength was unchanged in both limbs for both real and sham groups. Our results suggest that a single session of dual-tDCS before conventional physical therapy could improve sit-to-stand performance, which appeared to be improved over conventional physical therapy alone. However, strength performance was not increased after the combination treatment.

1. Introduction

Lower-limb functions are commonly disordered after stroke. However, despite classical rehabilitation techniques, the recovery of motor function after stroke is often incomplete. Transcranial direct current stimulation (tDCS) was introduced as a non-invasive tool to reversibly modulate brain excitability in humans. The use of tDCS has increased since the beginning of the 21th century. Its possible after-effects have led to increased interest in using tDCS for neurorehabilitation. A number of studies of stroke have reported that tDCS improved the performance of motor tasks and motor skills learning of the upper limbs [1,2]; however, only a small number of studies focused on lower-limb functions [1–3]. Using a higher current intensity (e.g., 2 mA) than that commonly used for the upper limb, 1 session of anodal tDCS over the M1 acutely enhanced the effect of motor practice of the paretic ankle [4], force production of the paretic knee extensors [5] and postural stability in patients with sub-acute stroke [6].

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After unilateral stroke, the excitability of the unaffected hemisphere is increased and an abnormally high interhemispheric inhibition drive from intact to lesioned hemisphere has been reported [7–9]. The enhanced neural activity of the contralesional motor areas prevents recovery of motor impairments during the subacute phase [10]. Anodal stimulation increases cortical excitability, whereas cathodal stimulation decreases cortical excitability. Dual-tDCS with anodal over the lesioned hemisphere and cathodal over the non-lesioned hemisphere has been used in unilateral stoke to restore brain excitability. Dual-tDCS seems to be a promising tool to enhance motor learning [11], with even greater ability to improve motor performance than unihemispheric tDCS in healthy adults [12,13]. In an imaging study, the corresponding tDCS-induced changes were reported to involve interhemispheric interactions [14]. One recent study reported improved walking speed immediately after a single session of dual-tDCS in sub-acute stroke patients [15].

Studies combining tDCS and training have found improved motor function over training alone [11,13,16–18]. However, the tDCS impact on motor performance varies widely, mostly because of differences in design/task/stimulation methods etc. Hence, meta-analyses did not report a significant improvement in motor performance with tDCS after stroke [19].

Little is known about the effects of dual-tDCS on the lower limb after stroke. The aim of the present study was to examine whether 1 session of dual-tDCS before conventional physical therapy (PT) modified clinical outcomes of lower-limb functions and how this compared to PT alone. The ability to transfer from sit-to-stand and to walk are the most commonly performed tasks of daily living and these are goals for rehabilitation after stroke. Our clinical outcomes were muscle strength and functional assessments that related to sit-to-stand and walking.

2. Methods

2.1. Participants

All included patients were first-ever diagnosed with cerebral infarction, confirmed by CT or MRI, with an onset of less than 6 months (mean [SD]: 3.2 [0.4] months). They had lower-limb weakness but were able to perform sit-to-stand independently and walk without physical assistance for at least 3 m. Participants were screened for exclusion criteria including the presence of intracranial metal implants, cochlear implants, cardiac pacemaker, history of seizures, no clear neurological antecedent history or psychiatric disorder, or excessive pain in any joint of the lower limb. A description of the study was provided to all participants and written informed consent was obtained from all before the experiments. The study protocol was approved by the local ethics committee of Mahidol University and registered at ClinicalTrials.gov (NCT03035162).

2.2. Experimental protocol

The study was conducted as a double-blind crossover sham-controlled trial. Each participant completed 2 sessions of experiments (real or sham) with an intervention interval of at least 1 week [17]. The 2 experiments were performed in random order for each participant. The experimental procedure is outlined in Fig. 1. Participants received PT for 1 h after dual-tDCS. In fact, the ideal timing for applying tDCS to maximize neuroplasticity and evoke behavioral changes has not been determined [19]. Even though a "during" training paradigm tends to have a better effect, we selected the "before" training paradigm for practical reasons because PT is much easier without the tDCS setup and tDCS before training has been shown to promote motor performance [20].

To determine lower-limb function, we examined strength and functional performance. Knee extensor strength was chosen because it is primarily required for performing sit-to-stand and walking. Strength was measured by using a Biodex system while participants comfortably sat in the position of knee flexed at 60° on the attached arm support. Participants performed 3 rounds of maximum voluntary contraction (MVC) of the knee extensor for 5 s separated by 2-min rests. The largest MVC was used for analysis. The data were observed in both deficient and normal limbs.

For functional assessments, the TUG and FTSST tests were chosen. The TUG, a simple and quick functional mobility test [21], was reported to be reliable and valid and correlated well with gait performance and walking endurance in stroke [22]. Participants were asked to sit on the chair and place their back against the chair. Timing began at "GO", the participants walked for 3 m, turned, walked back and sat down. Timing ended when the back was against the chair again. The FTSST test is commonly used to assess mobility and lower-limb acceleration [23]. It has also been introduced as an outcome measure for strength training and functional performance in stroke [24,25] and was reported to be reliable [26]. Participants were asked to stand up with the legs fully extended and sit down 5 times as quickly as possible. Timing began at "GO" and ended when the patient's buttocks touched the seat after the fifth sit-to-stand. Times were recorded in seconds. These outcome measures were evaluated before and after the intervention by a researcher who was blinded to the intervention.

2.3. Intervention

2.3.1. Transcranial direct current stimulation

Patients were seated with their arms comfortably supported to receive the stimulation. Skin preparation was required before applying the stimulation electrodes. A DC portable stimulator (HDC stim, Magstim, Wales, UK), programmed by an LCD touch screen (HDC prog), delivered a direct current through 2 rectangular saline-soaked sponge-pad electrodes with 35 cm^2 surface. An electroconductive gel was applied under the electrodes to reduce contact impedance. A 10–20 electroencephalography system [13] was used to apply anodal tDCS over the M1 of the affected hemisphere and cathodal tDCS over the M1 of the unaffected hemisphere, with the medial border of each electrode placed 5 mm lateral from the vertex. The current flowed continuously for 20 min during the real condition. For the sham condition, to provide stimulus sensation to participants, only 120 s was chosen because a duration of at least 3 min was previously found required to induce after-effects [27]. Current intensity was fixed at 2 mA because this was reported to induce changes in the excitability of deeper cortical structures innervating lower-limb muscles [28] and lower-limb spinal networks [29] and modulate the activity of the supplementary motor area involved in lower-limb performance, as explored by functional MRI [30]. tDCS was applied by a researcher who was blinded to the outcome assessment and data analysis.

Participants were asked about their feelings during tDCS. Eleven (58%) participants reported cutaneous sensations during real tDCS (3 itching and 8 tingling) and 3 (16%) reported tingling during the sham procedure. However, these sensations disappeared after tDCS removal. One participant experienced mild headache after tDCS, which resolved without any treatment within 24 h.

2.3.2. Conventional physical therapy

Participants received PT for 1 h under the guidance of a physical therapist with 10 years' experience in stroke rehabilitation, with blinding to the tDCS intervention. PT was administered to improve strength of the affected limbs including hip flexor, hip extensor,