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LOW-LEVEL INTERMITTENT QUADRICEPS ACTIVITY DURING TRANSCRANIAL DIRECT CURRENT STIMULATION FACILITATES KNEE EXTENSOR FORCE-GENERATING CAPACITY

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Abstract—Anodal transcranial direct current stimulation (tDCS) is known to increase the force-generating capacity of the skeletal muscles. However, when tDCS is concurrently combined with a motor task, interference may occur that hinders tDCS effects. Here, we tested the interaction and time course of tDCS effects on force production when paired with a low-level force-matching task. Twenty-two subjects were randomized into two groups: tDCS-Matching and tDCS-Resting. Each group received tDCS and a sham stimulation, separated by one week. Maximal knee extensor and flexor torques were measured before and up to twenty-five minutes following the stimulation. The tDCS-Matching group produced greater knee extension torques relative to sham when compared with the tDCS-Resting group. There was no significant effect for knee flexion. This suggests that interference does not occur for force production tasks when tDCS is combined with a motor task. Rather, the task appears to aid and isolate the effects to the muscle groups involved in the task.

Key words: noninvasive brain stimulation, functional specificity, metaplasticity, transcranial magnetic stimulation, voluntary torque, muscle strength.

INTRODUCTION

Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation technique that is capable of altering motor cortical excitability in a polarity-dependent fashion. For instance, anodal tDCS is known to increase cortical excitability (Nitsche and Paulus, 2000), which can enhance motor learning and movement control (Galea and Celnik, 2009; Reis et al., 2009; Schambra et al., 2011; Madhavan et al., 2011b; Kantak et al., 2012; Leenus et al., 2015). The effects of anodal tDCS have also been observed for force production, where existing research shows that a single bout of anodal tDCS significantly increases the force-generating capacity of the upper (Hummel et al., 2006; Krishnan et al., 2014; Abdelmoula et al., 2016) and lower extremity (Tanaka et al., 2009; Tanaka et al., 2011) muscles. These observations have strong clinical implications for recovery after neurological or orthopedic injury, where subjects are greatly impaired by muscle weakness (Pak and Patten, 2008; Bade and Stevens-Lapsley, 2012; Thomas and Stevens-Lapsley, 2012).

Evidence also indicates that interference (i.e., reduction or reversal of plasticity) may occur when tDCS is concurrently combined with a motor task, thereby hindering tDCS-dependent neuroplastic effects (Rosenkranz et al., 2000; Antal et al., 2007; Thirugnanasambandam et al., 2011; Bortoletto et al., 2015). Alternatively, some believe that *functional specificity*—where active neuronal networks are preferentially modulated—can be achieved with appropriate pairing of tDCS with a motor activity (Bikson et al., 2013; Cano et al., 2013). The interference effects of motor activity and its time course on force-generating capacity of a skeletal muscle have not been studied to date. This knowledge is important, as it would affect how tDCS can be applied in clinical and research settings. Therefore, this study investigated the interaction and longitudinal effects (i.e., time course) of anodal tDCS when paired with a force-matching task on force production of the thigh muscles. We hypothesized that tDCS when paired with a motor task would significantly *reduce* the force-generating capacity of the thigh muscles and that this effect would be specific to the muscles involved in the task.

EXPERIMENTAL PROCEDURES

Subjects and experimental design

Twenty-two able-bodied, healthy adults (seven women; mean age 22.8 ± 5.7 years) participated in this study after giving written informed consent, approved by the University of Michigan Institutional Review Board. All subjects were right leg dominant based on their

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Abbreviations: ANOVA, analysis of variance; MVIC, maximal voluntary isometric contraction; tDCS, transcranial direct current stimulation; TMS, transcranial magnetic stimulation.

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preferred leg to kick a ball (Krishnan and Williams, 2014; Krishnan, 2015). Subjects were included if they did not have a history of orthopedic or neurological conditions, psychiatric illness, or any contraindications to transcranial magnetic stimulation (TMS) or tDCS (Keel et al., 2001). Subjects were asked to refrain from exercising one day prior to testing.

Subjects were randomly assigned to one of two groups: tDCS-Matching (n = 10), where stimulation was administered while subjects performed a low-level force-matching task; or tDCS-Resting (n = 12), where stimulation was administered during rest. Each group participated in two testing sessions (tDCS and sham) separated by one week. The order of the stimulation protocol (either tDCS or sham) was randomly determined. An overview of the testing protocol can be found in Fig. 1.

Maximum voluntary isometric contraction (MVIC)

MVICs of the knee extensors and flexors were measured using a Biodex isokinetic dynamometer (System 4 Pro, Biodex Medical Systems, Inc., Shirley, NY, USA) according to the manufacturer's guidelines. The subject was seated on the dynamometer with their hip at 85° and knee at 70° of flexion, and was secured using the chest, waist, thigh, and shank straps of the device. Three submaximal (2 × 50% and 1 × 75% of perceived maximum) and one maximal contraction were then performed as practice trials for the knee extensors and flexors in an alternating fashion (i.e., extension followed by flexion). After a two-minute rest period, the subject performed two baseline MVICs of the knee extensors and flexors in an alternating fashion, with each like trial separated by two minutes of rest. MVIC trials were repeated after completing the tDCS or sham stimulation for every five minutes up to 25 min in order to evaluate the duration of tDCS effect on MVIC torques. Each MVIC lasted about four seconds and the position of the subject during testing was standardized by having them cross their hands across the chest and hold onto the chest straps during maximal contractions. Torque data were sampled at 1000 Hz using custom software written in LabVIEW 2011 (National Instruments Corp., Austin, TX, USA). A series of beeps cued the subject about when to start and end the MVICs. Visual feedback of their torque curves was provided through a computer monitor placed directly in front of the subject. No verbal encouragement was provided during the MVIC trials to minimize experimenter bias.

tDCS

TMS was employed to localize the M1 location of the leg for the application of tDCS. Single TMS pulses were delivered through an 110-mm double-cone coil attached to a Magstim 200^2 magnetic stimulator (Magstim Co Ltd, Whitland, UK) while the subject was seated on the Biodex dynamometer. The tDCS stimulation site was determined as the location at which TMS stimulation elicited the largest and most consistent knee extensor twitch torque at the lowest intensity when the subject performed a small background contraction of their quadriceps muscle (~5% of MVIC).

TDCS was applied for 12 min using a battery-driven stimulator, (Soterix 1 × 1, Soterix Medical INC, New York, NY, USA). The current was delivered at 2-mA intensity by a pair of carbon electrodes placed inside saline-soaked (0.9% NaCl) synthetic sponges (Soterix EASYpad, surface area: 5 × 7 cm^2), and secured using straps (Soterix EASYstrap). The anodal electrode was centered over the tDCS stimulation site while the cathode was placed on the right supraorbital area. For the *sham* condition, all procedures were identical to the active tDCS session, except that the current was ramped up/down to 2 mA at the start of stimulation (fade-in–short stimulation–fade-out approach) (Ambrus et al., 2012).

During tDCS, the subject was instructed to either rest or perform a force-matching protocol for the 12-min duration of the stimulation. The matching protocol required the subject to match their knee extension torque to a square wave with amplitude corresponding to 5% of their baseline MVIC value. The wave was present on the screen for 10 s, where the subject would match, and would then disappear for 20 s, prompting the subject to relax. Therefore, each subject in the tDCS-Matching group matched the target 24 times (Fig. 2).

Statistical analysis

All statistical analyses were performed using SPSS Windows version 22 (SPSS Inc., Chicago, IL, USA). MVIC torque values were divided by baseline values

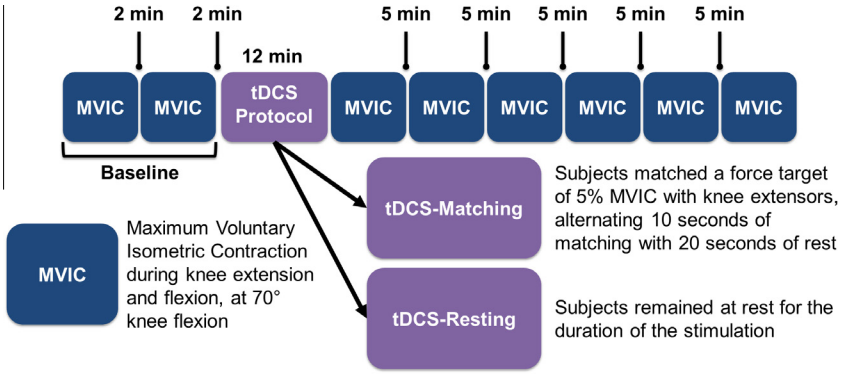

Fig. 1. Schematic of the experimental design.