



Task-specificity of unilateral anodal and dual-M1 tDCS effects on motor learning

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ABSTRACT

Task-specific effects of transcranial direct current stimulation (tDCS) on motor learning were investigated in 30 healthy participants. In a sham-controlled, mixed design, participants trained on 3 different motor tasks (Purdue Pegboard Test, Visuomotor Grip Force Tracking Task and Visuomotor Wrist Rotation Speed Control Task) over 3 consecutive days while receiving either unilateral anodal over the right primary motor cortex (M1), dual-M1 or sham stimulation. Retention sessions were administered 7 and 28 days after the end of training. In the Purdue Pegboard Test, both anodal and dual-M1 stimulation reduced average completion time approximately equally, an improvement driven by online learning effects and maintained for about 1 week. The Visuomotor Grip Force Tracking Task and the Visuomotor Wrist Rotation Speed Control Task were associated with an advantage of dual-M1 tDCS in consolidation processes both between training sessions and when testing at long-term retention; both were maintained for at least 1 month. This study demonstrates that M1-tDCS enhances and sustains motor learning with different electrode montages. Stimulation-induced effects emerged at different learning phases across the tasks, which strongly suggests that the influence of tDCS on motor learning is dynamic with respect to the functional recruitment of the distributed motor system at the time of stimulation. Divergent findings regarding M1-tDCS effects on motor learning may partially be ascribed to task-specific consequences and the effects of offline consolidation.

1. Introduction

The performance of nearly any voluntary motor task can improve with repetition and practice. Motor skill learning occurs not only during practice (online gains), but also between practice sessions (offline gains) (Müller et al., 2002; Robertson et al., 2005). Skill changes that occur offline are stabilised and enhanced through the process of consolidation, which can occur shortly after the end of training (Muellbacher et al., 2002). Following consolidation, motor skills can be maintained over longer periods of time and become increasingly automatic (retention). Rate and magnitude of skill acquisition are also highly task-specific, depending on complexity and nature of the task (e.g. Carey et al., 2005; Kuriyama et al., 2004).

In recent years, non-invasive neurostimulation studies have enhanced our comprehension of how brain areas are recruited across different learning phases and task demands. The primary motor cortex (M1) is known to modulate motor output and encode movement parameters, but there is increasing evidence to suggest that M1 is more acutely involved in the acquisition of motor skills (Galea et al., 2011; Matsuzaka et al., 2007; Ungerleider et al., 2002). It is well

documented that transcranial direct current stimulation (tDCS), with the anode over the M1 and the cathode over the contralateral supraorbital area, in combination with motor training results in greater motor performance gains compared with no stimulation. This has been reported across a range of motor tasks, measuring movement speed, accuracy and/or a change in movement kinematics. Some are broad clinical tests of hand function such as the Jebsen-Taylor Hand Function Test (Boggio et al., 2006; Williams et al., 2010), but most isolate a specific motor skill such as the serial reaction time task (SRTT) (Kang and Paik, 2011; Kantak et al., 2012; Nitsche et al., 2003), finger-sequencing tasks (Stagg et al., 2011; Vines et al., 2008b), ballistic thumb movements (Bortoletto et al., 2015; Galea and Celnik, 2009), maximal pinch force (Tanaka et al., 2009) and the sequential visual isometric pinch task (SVIPT) (Reis et al., 2013, 2009; Schambra et al., 2011).

These studies among others (e.g. Karni et al., 1995) support a prominent role of M1 in fast online performance gains. The aim of the present study was to stimulate M1 using tDCS over multiple motor learning sessions and different motor tasks. Only a few tDCS studies have probed the involvement of M1 in post-session motor learning

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processes. In one such study, Kantak et al. (2012) found that anodal tDCS applied to M1 during a SRTT improved online performance of a practised sequence and offline skill maintenance when tested the following day. In contrast, other studies found motor learning mediated by offline gains only. Reis et al. (2009) applied anodal tDCS during the SVIPT over the course of 5 days and participants showed significant learning between sessions, but not during sessions. Improvements were maintained at long-term retention 3 months later. These divergent findings may be explained by differences in the motor tasks applied and/or differences in training duration.

Recent evidence indicates that anodal tDCS to M1 may influence motor learning processes in a task-specific manner. Namely, Saucedo Marquez et al. (2013) compared the effects of tDCS on the acquisition of the finger-sequencing task and the adapted SVIPT over 3 consecutive days. While online and offline gains were reported for the finger-sequencing task, the SVIPT showed a learning effect only at retention, 1 week after the last training session. It was suggested that anodal tDCS necessarily has a stronger influence on neuronal firing rates in the area under the electrodes, which are functionally more relevant to some task demands than others. Since active stimulation of both motor cortices simultaneously (dual-M1 tDCS) has been associated with an increase in functional connectivity from intracortical areas to areas under the anode (Lindenberg et al., 2013; Sehm et al., 2013), this could have advantageous effects on tasks implicating more remote areas.

Dual-M1 tDCS has been under investigation as a powerful strategy to modulate motor performance (Vines et al., 2008a; Karok and Witney, 2013; Koyama et al., 2015; Waters-Metenier et al., 2014). Dual-M1 tDCS, with the anode over M1 and the cathode of the contralateral M1, is thought to induce up- and down-regulation of respective M1 cortical excitability (Karok and Witney, 2013; Mordillo Mateos et al., 2012; Williams et al., 2010). This has been shown to enhance motor learning in healthy subjects (e.g. Vines et al., 2008a) and to facilitate motor performance in stroke patients (e.g. Lindenberg et al., 2010). The exact mechanisms underlying dual-M1 stimulation effects on motor system activity are still incompletely understood. However, it appears to be more than a mere add-on of the anodal and cathodal currents. Resting-state and task-related functional magnetic resonance imaging (fMRI) studies examining the influence of tDCS on network activity found a decrease in interhemispheric functional projections in the conventional anodal and the dual-M1 condition, with only dual-M1 tDCS associated with increases in functional intracortical projections (Lindenberg et al., 2013; Sehm et al., 2013). Therefore, the currents may spread and activate the larger network, which suggests that dual-M1 stimulation effects could be manifested differently across different motor tasks.

The present study aimed to investigate task-specificity effects of unilateral anodal and dual-M1 electrode montages across various motor learning phases. In a sham-controlled, mixed-design, participants received motor training on three different tasks over three consecutive days while receiving either unilateral anodal, dual-M1 or sham tDCS. Two retention sessions, 7 days after the end of training and 28 days after the end of training, assessed how any performance changes are maintained over time. Participants trained on the Purdue Pegboard Test (PPT), a Visuomotor Grip Force Tracking Task and a Visuomotor Wrist Rotation Speed Control Task.

Based on previous research, we predicted that active tDCS would generally show enhanced motor learning compared to sham. We expected fast online gains in the PPT with marginal differences between electrode montages (Kidgell et al., 2013). We hypothesized slow and sustained motor learning effects with the Visuomotor Grip Force Tracking Task and the Visuomotor Wrist Rotation Speed Control Task, likely driven by offline gains (Reis et al., 2009; Saucedo Marquez et al., 2013; Waters-Metenier et al., 2014). Since dual-M1 tDCS is associated with different patterns of activation when compared with anodal tDCS (Lindenberg et al., 2013; Sehm et al., 2013), we expected different rates of skill acquisition in these tasks following multiple

stimulation sessions.

2. Materials and methods

2.1. Participants

Thirty healthy young adults (15 females; mean age 27.0 years $\pm$ 5.4 SD) participated in this study. All participants were right-handed, as determined by the Edinburgh Handedness Inventory (Oldfield, 1971) and were screened to be medically and neurologically healthy by a medical history questionnaire. The experimental protocol was performed in accordance with the revised Declaration of Helsinki and approved by the Faculty of Health Sciences Research Ethics Committee, Trinity College Dublin, Ireland. Informed consent was obtained from all individual participants included in the study.

2.2. Transcranial direct current stimulation

All stimulations except sham consisted of 15 min of 1.5 mA tDCS with a 10 s ramp period at the start and again at the end of stimulation (current density of 0.06 mA/cm²). In the sham group, current flow gradually increased over a 5 s interval until reaching the designated 1.5 mA and then ramped down after 10 s decreasing over a 5 s interval. TDCS was delivered via two flat electrodes covered by a saline-soaked sponge using a battery-driven, constant-current stimulator (NewRonika, Italy; HDCstim MI2011C002156).

Single-pulse transcranial magnetic stimulation (TMS) (Magstim, Whitland, UK; Rapid 2) was carried out at the start of the first session to determine the location of the first dorsal interosseous (FDI) 'hot-spots' in both M1s. Hot-spots were then marked on the scalp with permanent marker to ensure consistent electrode placement across the three consecutive days of stimulation. The FDI hand area was used as a central target in M1 to standardize electrode placements across participants. Prior to placing the tDCS electrodes on the scalp, participants' hair was brushed down when appropriate to remove any excess oil and clipped away from the target area with a plastic clip.

Since the current likely concentrates on the edges of the tDCS electrode (Faria et al., 2011; Minhas et al., 2011; Opitz et al., 2015), the front edge of the active electrodes was placed over the FDI hot-spots. The anode (25 cm²) was fixed over the FDI hand area in the right M1 in all stimulation groups. For the dual-M1 group, the front edge of the cathode (25 cm²) was placed over the FDI hand area in the left M1. A larger cathode (48 cm²) was fixed as a return (reference) electrode contralaterally at the fronto-orbital region for the anodal group so that stimulation of the prefrontal cortex was minimized. For the sham group, the electrode montage was randomly assigned for each participant to be the same as in either the anodal or dual-M1 group.

2.3. Purdue Pegboard Test (PPT)

The PPT (Lafayette Instrument, San Diego, USA; model 32020) is a standardised test of manual dexterity (Tiffin & Asher 1948) commonly used to assess hand function clinically. The task involves picking up small metal pins from a small rounded bowl with the left index finger and thumb and inserting as many as possible into a vertical array of holes. Standardised instructions were given to the participant, such as picking up only those pins, one at a time, that are in the bowl and not any that have spilled over. If a pin was dropped in transfer, a new pin had to be picked up from the bowl. In the ready position, seated directly in front of the PPT board with their left hand hovering over the bowl, timing began coinciding with the experimenter instruction to 'Go'. The time taken to complete the left array of holes on the pegboard was recorded, before replacing the pins into the bowl. Two administrations of the PPT constituted one block and performance was quantified as the average time from the two trials. Participants had the opportunity to practice with 5 pins at the start of each session.

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