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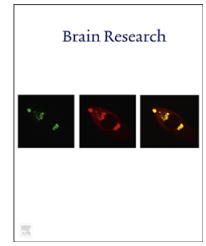

Research Report

Timing-dependent priming effects of tDCS on ankle motor skill learning

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ABSTRACT

Transcranial direct current stimulation (tDCS) has gained increasing interest in neurorehabilitation with its ability to modulate cortical excitability, and thereby influence neural plasticity and functional recovery. While the beneficial effects of tDCS on motor learning and function have been recognized, there is no clear consensus regarding the timing of the tDCS priming protocol in relation to the intervention especially with respect to lower limb motor learning. Depending on the time of priming in relation to the training task, the neural mechanisms of priming (gating vs. homeostatic plasticity) are different and thereby subsequently affect motor learning. Hence, the aim of this study was to examine the interaction of tDCS with subsequent vs. concurrent motor learning using an ankle visuomotor skill learning paradigm. Twelve healthy participants were tested under three stimulation conditions: (1) anodal tDCS prior to the motor task (tDCS-before), (2) anodal tDCS during the motor task (tDCS-during) and (3) sham tDCS during the motor task (tDCS-sham). Results revealed that tDCS application *during* practice of a skilled motor task increased motor performance compared to tDCS applied *prior* to motor practice. Both tDCS groups demonstrated enhanced motor learning when tested 24 hours after practice. We conclude that the priming effects of tDCS are timing dependent, and maybe a critical regulatory feature in determining outcomes of priming with tDCS.

1. Introduction

Neuroplasticity is the ability of the nervous system to reshape its anatomical and functional connectivity and properties in response to external or internal stimuli. Although the exact mechanisms associated with functional recovery after lesions of the nervous system are still unclear, neuroplasticity is considered a leading candidate mechanism associated with motor learning after neurological injury. As motor training alone is sometimes insufficient to meet functional demands of recovery after neurological injury, there is increasing research examining priming modalities such as transcranial direct current

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stimulation (tDCS) to increase the effectiveness of physical rehabilitation (Gomez Palacio Schjetnan et al., 2013; Madhavan and Shah, 2012; Schlaug et al., 2008). tDCS involves delivering continuous low intensity direct currents (0.5–2.0 mA) via surface electrodes attached to the scalp, to modulate activity of the cortical neurons in a polarity specific manner. Anodal tDCS can up regulate corticospinal excitability, indicated by an increase in mean motor evoked potential (MEP) amplitude (Nitsche and Paulus, 2000; Nitsche and Paulus, 2001) and when applied to the motor cortex (M1) during motor training results in improved motor performance and learning (Boggio et al., 2006; Nitsche et al., 2003; Reis et al., 2009; Zimerman et al., 2012) with retention of acquired skills as long as 3 months post stimulation (Reis et al., 2009). The physiological effects of tDCS are attributed to immediate changes to shifts in membrane potential, with after effects being induced by NMDA receptor modulations (Stagg and Nitsche, 2011).

Typically tDCS up-regulating protocols are paired with motor training to induce enhancements in motor learning (Geroin et al., 2011; Saucedo Marquez et al., 2013). Currently, there is no clear consensus regarding the timing of the tDCS priming protocol in relation to the intervention, as studies have applied tDCS both *before* motor training (Antal et al., 2011; Kuo et al., 2008; Stagg et al., 2009) and *during* motor training (Cuypers et al., 2013; Madhavan et al., 2011; Reis et al., 2009) resulting in large variations of the expected outcomes ranging from limited to large improvements. An increased understanding of state-dependent or metaplastic neuromodulation has led to the postulation that the likelihood of inducing synaptic modulation is contingent on the history of neuronal activity (Bienenstock et al., 1982; Jung and Ziemann, 2009; Turrigiano and Nelson, 2004). According to the Bienenstock–Cooper–Munro rule for homeostatic plasticity, a high level of prior synaptic activity will reduce the facilitatory effects of a concurrent facilitatory neuromodulatory protocol (and vice versa) and is related to changes in sensitivity of postsynaptic glutamate receptors. Another proposed mechanism for priming includes 'gating'. Gating occurs by disinhibition of intracortical inhibitory circuits as a result of increase in calcium in the targeted cortical neurons. Gating occurs instantaneously and is achieved *concurrently* with motor training (Ziemann and Siebner, 2008).

Hence the timing of stimulation relative to motor practice could be an important regulatory component of priming. Stagg et al. (2011) demonstrated that anodal tDCS applied *during* an upper limb sequence learning task enhanced the rate of learning compared to tDCS applied *before* practice. Thirugnanasambandam et al. (2011) demonstrated that short lasting voluntary hand contractions performed immediately *after* tDCS to the hand motor area reversed tDCS-induced motor cortical excitability. As studies examining state-dependent neuroplasticity of tDCS are limited, and relatively untested with respect to lower limb motor skill learning, we tested the interaction of tDCS with subsequent vs. concurrent motor learning. In accordance with the theory of homeostatic plasticity, we hypothesized that anodal tDCS *during* practice will result in enhanced motor performance and learning while tDCS applied *before* practice will inhibit motor learning.

Briefly, twelve participants were recruited and tested under three stimulation conditions: anodal tDCS prior to a motor task (tDCS-before), anodal tDCS during a motor task (tDCS-during) and sham tDCS during a motor task (tDCS-sham). We used a visuomotor tracking task to examine the time dependence of tDCS with respect to ankle motor skill learning (Madhavan et al., 2010; Madhavan et al., 2011). The accuracy of tracking the target sequence was calculated on a scale between 0–100, and was recorded as the accuracy index (AI) of motor performance. AI was tested before stimulation (PRE), 10 minutes post stimulation (POST10), 25 minutes after the end of stimulation (POST25) and 24 hours post practice (POST24h). To examine changes in the AI during practice, the average of every four minutes of tracking was calculated resulting in three practice bins (PRAC1, PRAC2, and PRAC3). Corticomotor excitability of the lower limb M1 was evaluated using single pulse transcranial magnetic stimulation (TMS) by recording motor evoked potentials (MEP) from the tibialis anterior (TA) muscle prior to stimulation (PRE), immediately post stimulation (POST0), and 25 mins after the end of stimulation (POST25). AI and MEP amplitudes were normalized to the respective baseline value by dividing the average practice and post values by the average baseline value for each participant.

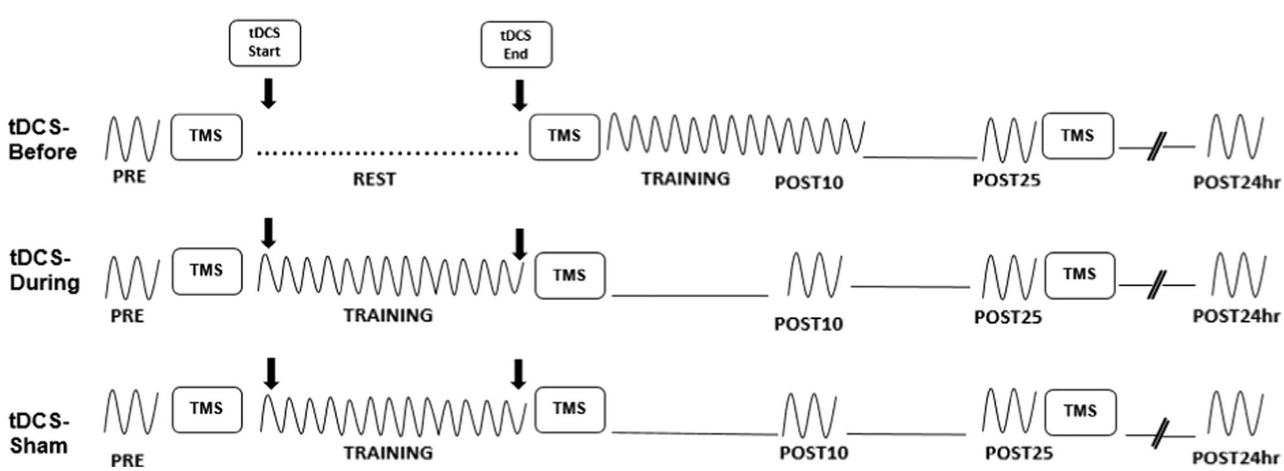

Fig. 1 – Schematic of study design. The waveform represents ankle tracking and boxes represent TMS testing.