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Research report

Cumulative effects of anodal and priming cathodal tDCS on pegboard test performance and motor cortical excitability

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HIGHLIGHTS

- atDCS during pegboard training improved motor performance.
- Preceding ctDCS induced an outlasting increase in cortical excitability.
- Preceding ctDCS improved off-line learning.
- Homeostatic plasticity is a possible factor for the cortical excitability effects.

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ABSTRACT

Transcranial direct current stimulation (tDCS) protocols applied over the primary motor cortex are associated with changes in motor performance. This transcranial magnetic stimulation (TMS) study examines whether cathodal tDCS prior to motor training, combined with anodal tDCS during motor training improves motor performance and off-line learning. Three study groups ($n = 36$) were trained on the grooved pegboard test (GPT) in a randomized, between-subjects design: SHAM—sham stimulation prior and during training, STIM1—sham stimulation prior and atDCS during training, STIM2—ctDCS stimulation prior and atDCS during training. Motor performance was assessed by GPT completion time and retested 14 days later to determine off-line learning. Cortical excitability was assessed via TMS at baseline (T0), prior training (T1), after training (T2), and 60 min after training (T3). Motor evoked potentials (MEP) were recorded from m. abductor pollicis brevis of the active left hand. GPT completion time was reduced for both stimulated groups compared to SHAM. For STIM2 this reduction in time was significantly higher than for STIM1 and further off-line learning occurred after STIM2. After ctDCS at T1, MEP amplitude and intracortical facilitation was decreased and intracortical inhibition was increased. After atDCS at T2, an opposite effect was observed for STIM1 and STIM2. For STIM2 these neuromodulatory effects were retained until T3. It is concluded that application of atDCS during the training improves pegboard performance and that additional priming with ctDCS has a positive effect on off-line learning. These cumulative behavioral gains were indicated by the preceding neuromodulatory changes.

1. Introduction

From our experience we know that practicing a new motor task improves motor performance and that an acquired skill remains relative stable without additional practice. However the performance gains achieved within a certain training period are limited. This obviously depends on straits to reorganize cortical networks [1], but also on the utilization of cognitive resources at the early stage of motor learning [2]. Recently noninvasive brain stimulation has been probed successfully in order to enhance motor performance at various hand motor learning tasks. Often transcranial direct current stimulation (tDCS) was used in such studies [3], a technique that allows polarization of membrane potentials [4,5] and modulation of cortical excitability [6].

Basically tDCS induces a current flow through the skull, and it was suggested that cathodal polarization slightly decreases firing rate in the underlying brain tissue while anodal polarization slightly increases the firing rate [4]. After application of tDCS over the

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primary motor cortex such neuromodulatory effects can be observed via transcranial magnetic stimulation (TMS): after cathodal tDCS (ctDCS) cortical excitability decreases and after anodal tDCS (atDCS) excitability it increases [7,8]. For these effects transient changes in synaptic efficacy are held responsible. For example it was demonstrated with magnetic resonance spectroscopy that atDCS (1 mA, 10 min) locally reduces GABA, while ctDCS reduces glutamergic activity [9].

If tDCS is paired with motor learning it is crucial to consider timing and polarity of stimulation. In several studies atDCS was tested during practice in order to facilitate motor performance [10–12]. It is argued that increase of firing rates in task specific networks imposes additional strengthening of specific synaptic connections [13]. In some studies further priming tDCS (tDCS in advance of practice) was tested. Stagg et al. [14] found slower learning of a finger sequence task for both atDCS and ctDCS, while Antal et al. [15] found an improvement in early learning of a visuomotor coordination task for both polarities. Despite these inconsistencies in learning paradigms, lowering of neuronal activity with priming ctDCS seems to be advantageous as it reduces the threshold for subsequent protocols to increase cortical excitability [16,17]. Also the site of stimulation has to be considered. At tasks with high cognitive demands the anode often is placed over the premotor cortex [18,19], while at tasks depending more on sensory input placement over the primary motor cortex showed appropriate [10,12,20].

In most of the studies the impact of tDCS has been exclusively explored at the behavioral level. However to elucidate the underlying adaptive processes, it is advantageous to incorporate noninvasive neuronal measures. Therefore in the current study we measured motor evoked potential (MEP) amplitudes in order to evaluate changes of cortical excitability. As training paradigm the grooved pegboard test (GPT) was chosen. It was shown that the GPT itself evokes rather minor excitability changes [21,22] and therefore the tDCS-induced changes should dominate the picture. The study protocol was designed in order to examine whether ctDCS prior to motor training, combined with atDCS during motor training, cumulatively enhances pegboard test performance and off-line learning. We further assume that the atDCS and priming ctDCS driven changes in cortical excitability are related to the expected behavioral gains. To verify these assumptions three matched study groups were tested in a randomized, single-blind, between-subject design: one group receiving sham stimulation prior and during GPT training, a second group receiving sham stimulation prior and atDCS during the training and a third group receiving ctDCS prior and atDCS during the training. For all three groups single and paired pulse TMS assessments were performed prior to priming stimulation (sham or ctDCS), after priming stimulation, immediately after practice, and 60 min after practice. To assess off-line learning GPT performance was retested two weeks later.

2. Material and methods

2.1. Participants and study design

Thirty-six healthy volunteers took part in the study approved by the Ethics Committee at the Medical University of Graz. They were screened for possible neurological disorders and contraindications to TMS and signed a written informed consent. All participants were right-handed according to the laterality quotient (LQ) from the Edinburgh Handedness Inventory [23]. According to self report none of the participants actively played an instrument or engaged in any other activity that extensively involved the left non-dominant hand. Following acquisition of a novel task the same subject could not be tested again, thus the participants were randomly assigned to three study groups, ($n = 12$) each receiving different tDCS protocol. The first group (8 ♀ and 4 ♂, mean age 24.92 ± 5.04 years) underwent sham tDCS (SHAM). The second group (8 ♀ and 4 ♂, mean age 27.67 ± 9.98 years) underwent sham stimulation preceding the GPT and atDCS during the GPT performance (STIM 1). The third group (6 ♀ and 6 ♂, mean age 26.00 ± 8.91 years) underwent ctDCS preceding GPT and atDCS during GPT performance (STIM2).

2.2. Grooved Pegboard test and skill training

The use of GPT (Model 32025, Lafayette Instrument, USA) is well documented for the ability to generate performance curves and is also used to assess motor function in patients with motor deficits. In this study, the GPT was performed in 4 blocks (4 trials in each block) with interblock rest intervals of 2 min to avoid muscle and central fatigue. The GPT was retested two weeks after skill training in a single block (4 trials). Subjects received exact instructions and a demonstration of the test, without being provided with practice trials. All participants completed the test at equal ambient conditions at the same time of day (between 9 and 12 a.m.). The observer instructed the subjects to complete the task as fast as possible and recorded the time for each trial.

2.3. Transcranial direct current stimulation (tDCS)

A bipolar electrode montage was utilized to deliver tDCS. The active electrode was placed to stimulate the right primary motor cortex M1, contralaterally to the performing left hand. The electrode was centered on C4 of the international 10–20 electroencephalogram system as it was shown in neuroimaging studies that C3/C4 corresponds to the left and right M1 [24]. The correspondence between C4 and right M1 was additionally confirmed using TMS individually for each subject and adjusted when necessary to the APB representation spot. The reference electrode was placed over the contralateral left supraorbital area. tDCS was delivered by the MAGSTIM ELDITH DC-stimulator and a pair of non-metallic, conductive rubber electrodes with water-soaked synthetic sponges ($5\,cm \times 7\,cm/35\,cm^2$). Stimulations were delivered at an intensity of 1 mA (current density $0.029\,mA/cm^2$). As it was shown that a stimulation period between 9 to 20 min is appropriate to induce stable after effects in the motor cortex [25], priming ctDCS was applied for 15 min. The period of atDCS during GPT practice was approximately 20 min in order to cover the overall training period. For sham tDCS the electrodes were placed in the same manner, however the stimulation was turned off after 15 s [16]. This procedure allows to blind subjects for the stimulation condition [10].

2.4. TMS assessments

For the TMS assessment, two Magstim 200 magnetic stimulators connected via a Bistim module (The Magstim Company, Whitland, Dyfed, UK) were employed. Magnetic pulses were delivered through a figure eight-shaped coil (outer loop diameter of 9 cm). The coil was positioned on the scalp over the right motor cortex at the optimal site for stimulating the contralateral left abductor pollicis brevis (APB). The intersection of the coil was placed tangentially to the scalp, with the handle pointing backward and laterally at a 45° angle away from the midline. The resting motor threshold (rMT) was expressed as a percentage of the maximum output of the stimulator. Using suprathreshold intensities, the coil was moved over the scalp in small steps to locate the site with the largest MEP. This position was marked on an EEG cap and the coil was fixed at that position.

The resting motor threshold (rMT), MEP, short-latency intracortical inhibition (SICI) and intracortical facilitation (ICF) were examined. The resting MT was defined as the lowest stimulus