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Effects of Different Electrical Brain Stimulation Protocols on Subcomponents of Motor Skill Learning

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ABSTRACT

Background: Noninvasive electrical brain stimulation (NEBS) with transcranial direct current (tDCS) or random noise stimulation (tRNS) applied to the primary motor cortex (M1) can augment motor learning.
Objective: We tested whether different types of stimulation alter particular aspects of learning a tracing task over three consecutive days, namely skill acquisition (online/within session effects) or consolidation (offline/between session effects).
Methods: Motor training on a tracing task over three consecutive days was combined with different types and montages of stimulation (tDCS, tRNS).
Results: Unilateral M1 stimulation using tRNS as well as unilateral and bilateral M1 tDCS all enhanced motor skill learning compared to sham stimulation. In all groups, this appeared to be driven by online effects without an additional offline effect. Unilateral tDCS resulted in large skill gains immediately following the onset of stimulation, while tRNS exerted more gradual effects. Control stimulation of the right temporal lobe did not enhance skill learning relative to sham.
Conclusions: The mechanisms of action of tDCS and tRNS are likely different. Hence, the time course of skill improvement within sessions could point to specific and temporally distinct interactions with the physiological process of motor skill learning. Exploring the parameters of NEBS on different tasks and in patients with brain injury will allow us to maximize the benefits of NEBS for neurorehabilitation.

Introduction

A substantial portion of our lives is spent learning new motor skills: from walking to writing, driving and sports. Motor skills are the primary mechanism for interaction with the world around us; hence, defective motor skills resulting from neurological diseases are a severe impairment. Noninvasive electrical brain stimulation (NEBS) applied transcranially to the motor cortex (M1) has been shown to improve motor skill learning in healthy individuals [1,2] and in chronic stroke patients [3–5]. Transcranial direct current stimulation (tDCS) with an anode over M1 and a cathode over the contralateral supraorbital area, in combination with motor training resulted in greater skill gains compared to sham in healthy subjects. Using tasks of different complexity, experiments have shown both within session (online) improvements in a single-day [6,7], as well as between session (offline) improvements observed with multi-session training [8,9]. In an attempt to maximize stimulation benefits, recent studies utilized a bilateral M1 montage, with an anode over the M1 contralateral and a cathode ipsilateral to the training hand. The basic idea of this approach is the modulation of interhemispheric inhibition [10–12], that is strengthening the facilitatory effect on one M1 with anodal tDCS, while reducing the inhibitory influence of the other M1 by cathodal tDCS [12,13].

While tDCS uses a direct current flowing in one direction necessitating an anode and cathode with potentially different local effects, transcranial random noise stimulation (tRNS) uses an alternating current with a randomly changing frequency and current direction, removing anode/cathode-specific effects. High frequency tRNS (100–640 Hz) applied to M1 has also been shown to facilitate implicit motor sequence learning [14]. Both anodal tDCS and tRNS enhance M1 excitability [14–16], although it is likely

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there are differences in the mechanism of action of a constant current versus changing currents applied to the cortex [17,18]. It has been suggested that the concept of stochastic resonance may apply to all forms of NEBS: stimulation-induced noise introduced to a neuronal system may provide a signal processing benefit in the brain by altering the signal-to-noise ratio [19,20]. While synchronization with task–relevant activity may play a particular role for tRNS, additional homeostatic mechanisms induced by a constant noise input may apply for tDCS [19,21]. Despite the huge amount of separate investigations of tDCS and tRNS effects assessed in a single session, there are only two direct comparisons between these stimulation types: For visuomotor learning, neither tRNS nor anodal tDCS applied to M1 combined with a brief single training session improved learning relative to sham stimulation [22]. On an orientation discrimination task Pirulli et al. [23] found the effect of stimulation type applied to the visual cortex varied depending on the timing of stimulation, with tRNS more effective if applied during practice, whereas tDCS induced better discrimination when applied before practice. However, these results directly contrast with results from the motor learning domain, where anodal tDCS applied to M1 before learning a serial reaction time task was found to inhibit or leave unaffected subsequent learning [7,24], showing NEBS effects are current type, site and task specific.

Given that these studies probed aspects of learning in a single session and one was not directly related to motor learning, it is currently unknown whether tDCS and tRNS would exert distinct effects onto specific subcomponents of motor skill learning, i.e. within session (online) improvements or between session (offline) effects, only assessable when training for more than one session. Disentangling how different forms of NEBS interact with the stages of the learning process is of great value both for understanding the mechanisms of motor skill learning as well as to maximize clinical benefits of NEBS. Here, we directly contrast the effects of tDCS and tRNS on repeated motor learning sessions in an exploratory study to test the efficacy of these different stimulation types.

Methods and materials

This study was in accordance with the Declaration of Helsinki amended by the 59th WMA General Assembly, Seoul, October 2008 and was approved by the local Ethics Committee of the University of Freiburg.

Participants

Subjects were invited for participation by bulletin board announcements at the university as well as by word-of-mouth and social media. 91 healthy, adult participants (39 males, mean age = 25.7, SD = 4.6 years) were recruited to the experiment and given a small monetary reimbursement. All participants gave written informed consent, and met safety criteria for TMS and tDCS [25]. All were right handed as assessed by the Edinburgh Handedness Inventory (mean score = 93.4, SD = 10.7). Inclusion required a normal neurological or psychiatric medical history. Subjects were also screened for symptoms of depression using the Beck Depression Inventory ([26], score $>$ 12 leading to exclusion). In addition, all subjects were screened for the brain-derived neurotrophic factor (BDNF) val66met polymorphism known to affect motor skill learning [27] and the distribution of genotypes (val66val, Met carriers) within each stimulation group was monitored to avoid a confounding effect in a particular stimulation group. Subjects were not excluded due to their genotype.

The tracing task

We created a complex, continuous word/shape tracing task with the Psychophysics Toolbox package [28,29] for Mathworks MATLAB, on the basis of established hand tracing tasks [30–32]. Participants were required to trace over a series of words and shapes on a Wacom Bamboo Fun graphics tablet with a stylus held in the non-dominant (left) hand. The non-dominant hand was selected in order to increase task difficulty for a steeper learning curve. The template letters were presented separately on a monitor (Fig. 1A and B). Participants could move the cursor to a ready position by moving the stylus without touching the tablet; touching initiated the trial and started a time bar showing how long was left for the trial. Each trial allowed 2 s per real letter or shape letter (e.g. 10 s for a 5 letter word). This timing was selected from speed accuracy trade-off data from a behavioral pilot, finding 2 s per letter difficult but not frustrating. Instructions were to trace as accurately as possible over the template using all of the given time and lift the stylus on finishing a trial, allowing us to measure the time taken per trial.

Template words consisted of the most common 3–5 letter German words selected from a free database (compiled from subtitles by Invoke IT Limited, http://invokeit.wordpress.com/frequency-word-lists/) which were screened to remove emotionally salient words. Words were printed in a freely available cursive font (League Script, www.theleagueofmoveabletype.com). For template shapes, an alphabet of random shapes was drawn in Inkscape (http://www.inkscape.org/), where each shape corresponded to each letter of the alphabet. Using this, each real word was converted into a 'shape word,' where each real letter was replaced by a made-up shape. For instance, the word 'der' (Fig. 1A) was turned into a shape-word with shape-letters corresponding to each real letter (Fig. 1B). A single trial consisted of tracing over one template (one real word or one shape-word).

Scoring method

To measure participants' performance, we devised a scoring method which allowed for intuitive feedback and analysis. In brief, the final score can be interpreted as 'percentage correct': a participant's trace which perfectly matches the template receives a score of 100; any deviation from this (drawing off the template lines) reduces the score. Drawing very little or consistently far away from the target lines results in a score at or approaching zero.

In order to calculate these scores, both the trace and template (target) data was converted into an image (Fig. 1C and D). The sum of the differences between the two images was used as scoring method (Fig. 1E). In order to introduce a margin of error, both images were blurred with a Gaussian kernel (size: 50 × 50 pixels; standard deviation: 12 pixels; Fig. 1C and D) – this allows minor deviations, and makes the score worse the further the trace deviates from the target, with a cut-off if deviations are too far. At this point, a perfect trace gives 0 and deviations are arbitrarily high. Therefore, we set the sum of the pixels in the template image as a threshold upper score (e.g. writing nothing is the baseline for worst score). The score was thresholded at this number, then divided by it and subtracted from 1. This gives a fraction (with 0 as the worst score and 1 as the best), which we turned into a percentage.

Study design

The study design is shown in Fig. 2. We chose a parallel study design. Subject allocation to one of the four stimulation conditions followed a fully balanced randomization list prepared prior to the experiment. The electrode montage was known to both participant