Relationship Between Non-invasive Brain Stimulation-induced Plasticity and Capacity for Motor Learning

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ABSTRACT

Background: Cortical plasticity plays a key role in motor learning (ML). Non-invasive brain stimulation (NIBS) paradigms have been used to modulate plasticity in the human motor cortex in order to facilitate ML. However, little is known about the relationship between NIBS-induced plasticity over M1 and ML capacity.

Hypothesis: NIBS-induced MEP changes are related to ML capacity.

Methods: 56 subjects participated in three NIBS (paired associative stimulation, anodal transcranial direct current stimulation and intermittent theta-burst stimulation), and in three lab-based ML task (serial reaction time, visuomotor adaptation and sequential visual isometric pinch task) sessions.

Analysis: After clustering the patterns of response to the different NIBS protocols, we compared the ML variables between the different patterns found. We used regression analysis to explore further the relationship between ML capacity and summary measures of the MEPs change. We ran correlations with the "responders" group only.

Results: We found no differences in ML variables between clusters. Greater response to NIBS protocols may be predictive of poor performance within certain blocks of the VAT. "Responders" to AtDCS and to iTBS showed significantly faster reaction times than "non-responders." However, the physiological significance of these results is uncertain.

Conclusion: MEP changes induced in M1 by PAS, AtDCS and iTBS appear to have little, if any, association with the ML capacity tested with the SRTT, the VAT and the SVIPT. However, cortical excitability changes induced in M1 by AtDCS and iTBS may be related to reaction time and retention of newly acquired skills in certain motor learning tasks.

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Introduction

The ability to learn new motor skills is dependent on brain plasticity, the ability of the human brain to make changes in its structure or function [1–3]. Long-term potentiation (LTP) and long-term depression (LTD) have been proposed as the principal mechanism of such learning [4,5]. LTP and LTD-like changes in cortical excitability can be induced by non-invasive brain stimulation techniques (NIBS) such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) [6–9]. The above-mentioned NIBS protocols have been applied to different cortical areas, but mostly commonly to the primary motor cortex (M1) due to the putative role of this area in motor learning processes [10]. The most frequently used procedure to evaluate the effects induced by those techniques is to measure the changes in the amplitude of the motor evoked potentials (MEPs) from the primary motor cortex (M1) before and after NIBS paradigms. Excitatory paired associative stimulation (PAS) [11], anodal transcranial direct current stimulation (AtDCS) [12] and intermittent theta burst stimulation (iTBS) [13] are some examples of NIBS protocols that have been reported to induce a facilitation in the MEPs for periods up to 1 h post-stimulation.

Stimulation of M1 by NIBS has been reported to enhance performance and learning in healthy subjects in a variety of motor tasks such as implicit learning [14], visuomotor learning [15,16] and skill learning [17] tasks (for a review see Refs. [18,19]).

These effects of NIBS are believed to involve or augment the same mechanisms involved in the motor skill learning process, and are a key argument in utilizing NIBS in rehabilitation (e.g., in Stroke) [20].

However, little is known about the relationship between the plasticity induced by these NIBS protocols, performance on motor learning tasks, and retention of newly acquired skills. Therefore, the main goal of this study is to explore whether the cortical plasticity induced by NIBS protocols on M1 correlates with the motor learning capacity as measured by performance on established lab-based motor learning tasks.

We applied AtDCS, PAS and iTBS over the left motor cortex in a total of 56 subjects. We then measured performance and retention on three well-established motor learning capacity measures: implicit motor learning, visuomotor adaptation and skill learning.

Methods

Subjects and general procedure

A total of 56 Caucasian subjects (50 men; 53 right-handed; mean age 20.52 ± 1.52), who had already participated in a previous NIBS study in our lab [21] were recruited after giving written informed consent. Subjects were not screened for particular patterns of responsiveness either to training or stimulation protocols in prior experiments. The experiments were approved by the Ethics Committee of the University of A Coruña and are in accordance with Declaration of Helsinki.

The subjects participated in 3 sessions of NIBS, with at least seven days between sessions. The order of the NIBS sessions was counterbalanced between subjects. A minimum of one week after the last NIBS session, subjects participated in the serial reaction time task (SRTT), visuomotor adaptation task (VAT) and sequential visual isometric pinch task (SVIPT). Each participant was invited to participate in all three behavioral tasks. Each behavioral task session was conducted at least one week apart. 100% of the sample performed the SRTT and the VAT while 78.6% completed the SVIPT. The order of motor learning studies was counterbalanced between subjects. Each individual subject took part in all sessions at the same time of day.

TMS procedure

TMS was delivered through a figure-of-eight coil with an outer diameter of 70 mm (Magstim Co., Whitland, Dyfeld, UK) over the left motor cortex. The coil was held with the handle pointing backwards and laterally to evoke an anteriorly directed current in the brain, and was optimally positioned to obtain MEPs in the contralateral FDI. Single and paired pulses were delivered from a monophasic Magstim BiStim.

For all three protocols, baseline and outcome data were collected in an identical fashion (see Fig. 1). For a more detailed description refer to Ref. [21].

NIBS protocols

Parameters of PAS, AtDCS and iTBS are described in Table 1. For more information on NIBS and EMG recording parameters refer to Ref. [21].

We make special note of the fact that the PAS protocol employed involves heterotopic stimulation, pairing FDI and ulnar nerve stimulation. This is not the most common protocol employed for PAS, and thus results may not be generalizable to the original PAS protocol pairing APB and median nerve stimulation. However, several studies have reported that it too induces changes in MEP amplitude, similar to the original PAS protocol [22,23].

Serial reaction time task (SRTT)

Subjects were seated in front of a computer screen (46 × 29 cm) at eye level behind a keyboard on the table with four colored keys (letters "j," "k," "l" and "ñ"; from now on we will refer to them as "1," "2," "3" and "4," respectively). They performed an SRTT [24] running on SuperLab (version 4.0). They were instructed to push each key with a different finger of the right hand (index finger for "1," middle finger for "2," ring finger for "3," and little finger for "4").

An asterisk appeared in one of four positions that were horizontally spaced on a computer screen and permanently marked by black squares on a white screen background.

Each screen position corresponded to a key on the keyboard. The spatial configuration of the keys was fully compatible with the screen positions. Subjects were instructed to press the corresponding key as fast as possible. The stimuli disappeared immediately after pushing any key, and appeared again after 500 ms.

Before starting the SRTT experiment, a practice block with 60 trials in random order was administered to ensure that participants understood the instructions.

SRTT consisted of eight test blocks of 120 trials each (preceded by a practice block of 60 trials in pseudorandom order). In test Blocks 1 and 6 (random "R" blocks), the sequence of asterisks followed a pseudorandom order. For both blocks asterisks were presented with equal frequency in each position, the sequence could not contain runs of four units (e.g., 1234 or 4321) or trills of four units (e.g., 1212). In Blocks 2–5 and 7–8 (sequence "S" blocks), the same 12 unit sequence of asterisk positions repeated itself 10 times (121423413243). Retention was measured in two additional sessions, 45 min and 24 h after the completion of the first session. Both retention sessions were identical and consisted of three blocks: Block 1 was a random block, while the second and third blocks were sequence blocks. Subjects were not told about the repeating sequence.
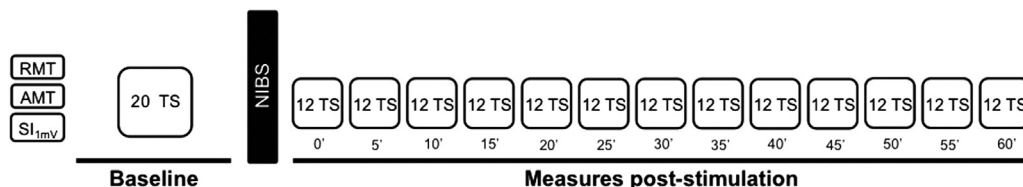
Figure 1. Common protocol for each NIBS session. Resting Motor Threshold (RMT), Active Motor Threshold (AMT), Stimulus intensity to elicit a 1 mV (SI$_{1mV}$) peak-to-peak amplitude Motor Evoked Potential (MEP) were recorded. 20 Baseline MEP's (at SI$_{1mV}$). After each protocol was delivered, MEP amplitude was measured at 5-min intervals for 60 min. Modified from Ref. [21] (with permission).