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Task-specific effect of transcranial direct current stimulation on motor learning

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Transcranial direct current stimulation (tDCS) is a relatively new non-invasive brain stimulation technique that modulates neural processes. When applied to the human primary motor cortex (M1), tDCS has beneficial effects on motor skill learning and consolidation in healthy controls and in patients. However, it remains unclear whether tDCS improves motor learning in a general manner or whether these effects depend on which motor task is acquired. Here we compare whether the effect of tDCS differs when the same individual acquires (1) a Sequential Finger Tapping Task (SEQTAP) and (2) a Visual Isometric Pinch Force Task (FORCE). Both tasks have been shown to be sensitive to tDCS applied over M1, however, the underlying processes mediating learning and memory formation might benefit differently from anodal transcranial direct current stimulation (anodal-tDCS). Thirty healthy subjects were randomly assigned to an anodal-tDCS group or sham-group. Using a double-blind, sham-controlled cross-over design, tDCS was applied over M1 while subjects acquired each of the motor tasks over three consecutive days, with the order being randomized across subjects. We found that anodal-tDCS affected each task differently: the SEQTAP task benefited from anodal-tDCS during learning, whereas the FORCE task showed improvements only at retention. These findings suggest that anodal-tDCS applied over M1 appears to have a task-dependent effect on learning and memory formation.

Introduction

Repeated practice of a motor task induces skill learning, which is manifested as increasingly efficient movement execution (Luft and Buitrago, 2005). Depending on the task, skill learning might require days, weeks, or months of training. For example, a simple motor task that involves sequential finger movements will show improvements within minutes (Karni et al., 1995) while learning to play an instrument will require years of frequent practice (Dayan and Cohen, 2011). Once the motor task is acquired, performance can diminish again over time if practice is discontinued (Luft and Buitrago, 2005; Reis et al., 2009). At least three different but interconnected processes have been identified during motor skill learning: (1) practice effects resulting in performance gains during a training session (online gains); (2) memory consolidation occurring between sessions, i.e., during a period of rest or sleep making the acquired memory resistant against interference (offline effects) (Robertson et al., 2005; Reis et al., 2009), and (3) long-term memory formation as indicated by successful retention after days, weeks, or months (long-term retention).

Neural models of motor learning have generally converged toward the notion that different brain regions are recruited depending on the learning phase and the acquired task. Practice resulting in fast online gains triggers neuroplastic changes within the primary motor cortex (M1) and premotor areas, which are additionally modulated by executive functions and reward mechanisms. These changes are characterized by increased prefrontal activity, typically observed early in learning (Sanes, 2003), and by error-correction processes mediated by the cerebellum (Penhune and Steele, 2012). Interestingly, these mechanisms seem to be rather independent of the practiced motor task. By contrast, it has been proposed that consolidation of motor memories involves areas which are task-specific such that sequence learning relies strongly on cortico-striatal circuits, whereas sensorimotor adaptation relies predominantly on cortico-cerebellar pathways (Doyon and Benali, 2005; Doyon et al., 2009). If training continues over a longer period of time, movements become increasingly automatized and long-term representations are formed which are thought to rely on M1, premotor, and parietal areas (Doyon and Benali, 2005; Doyon et al., 2009; Penhune and Steele, 2012).

Recent studies have shown that anodal transcranial direct current stimulation (anodal-tDCS) results in increased corticomotor excitability when M1 is stimulated at rest (Nitsche and Paulus, 2000). Applying anodal-tDCS to M1 during online or offline processes has been shown to facilitate motor learning despite methodological differences across studies (for an overview, see Table 1). Interestingly, the beneficial effect of anodal-tDCS has been demonstrated for a large number of motor tasks (as

shown in Table 1) such as explicit finger sequencing (Stagg et al., 2011), serial reaction time tasks (SRTTs) (Nitsche et al., 2003; Tecchio et al., 2010; Kantak et al., 2012), sequential visual isometric pinch force control (Reis et al., 2009; Schambra et al., 2011), the Jebsen Taylor hand function test (Boggio et al., 2006), ballistic thumb movements (Galea and Celnik, 2009), and reaching adaptation tasks (Galea et al., 2011). For serial reaction time and sequential pinch force control tasks it was further shown that applying anodal-tDCS to premotor areas has similar facilitating effects on learning (Kantak et al., 2012; Vollmann et al., 2013).

TABLE 1

Table 1. **Summary of anodal-tDCS studies stimulating primary motor cortex aiming to improve motor sequence learning in healthy populations (all in right-handed participants)**.

Two of these previously mentioned transcranial direct current stimulation (tDCS) studies have compared all three learning processes directly (Reis et al., 2009; Kantak et al., 2012) but revealed divergent results even though both studies applied tDCS during the training sessions (i.e., targeting online gains): Reis et al. (2009) showed that anodal-tDCS enhanced skill acquisition of an *isometric pinch force task*, which involved learning to control a force transducer in order to move a cursor displayed on a computer screen through a sequence of five horizontal targets. Training of this task occurred over a period of 5 days. The beneficial effect of anodal-tDCS mainly emerged through an effect on offline gains between sessions (offline effects), and was still present at a long-term retention test (RT) taking place up to 3 months after acquisition. Conversely, a *SRTT*, in which a sequence of key-presses was cued visually, did not show offline effects (Kantak et al., 2012). Instead, anodal-tDCS boosted behavioral improvement during training (online gains) which resulted in improved performance on a RT 1 day later.

This previous work suggests that applying anodal-tDCS to M1 influences online, offline, and long-term retention processes in a task-specific manner. This is in line with the proposal that depending on the task characteristics and attentional demands (Hazeltine et al., 1997), online and offline processes occurs either predominantly in M1 or rely critically on neuroplasticity in other areas such as the cerebellum or basal ganglia. Evidence for task-specificity of tDCS was revealed by Galea et al. (2011) who showed that a visual adaptation task was differentially influenced by anodal-tDCS over M1 versus the cerebellum. Alternatively, it could be argued that the differences between the

studies of Reis et al. (2009) and Kantak et al. (2012) were due to a difference in training duration that consisted either of multiple days of practice (Reis et al., 2009) or one single training session (Kantak et al., 2012). A lack of multisession tDCS studies in the field of motor skill learning, and methodological differences regarding stimulation parameters makes it difficult to draw clear conclusions on these controversial results.

Here, we investigate whether the beneficial effect of anodal-tDCS on online gains, offline effects, and long-term retention after multiple days of motor practice is task-specific. Each participant acquired a modified version of the sequential isometric visual pinch force task (FORCE) similar to that of Reis et al. (2009) and a Sequential finger tapping task (SEQTAP) (Walker et al., 2003). The tasks were trained either with anodal-tDCS applied over M1 (experimental group) or with sham-tDCS (control group). Both tasks have been previously presented in the tDCS literature but, to the best of our knowledge have never been directly compared to each other over multiple sessions. In particular, we tested the effects of tDCS on the three different phases influencing motor skill learning (i.e., online gains, offline effects, and long-term retention).

Based on previous research (Nitsche et al., 2003; Reis et al., 2009; Schambra et al., 2011; Stagg et al., 2011; Kantak et al., 2012) we predicted that the anodal-tDCS group would show enhanced motor skill learning compared to the control group in both tasks. However, it is uncertain whether anodal-tDCS effects on (i) online gains, (ii) offline gains, or (iii) long-term retention are task-specific because motor skill learning represents a complex cognitive process relying on a number of different areas in addition to M1, such as premotor and supplementary motor cortex, the cerebellum and the basal ganglia (Ungerleider et al., 2002). Further understanding of how tDCS affects motor skill learning could have clinical implications, as tDCS is increasingly considered as an adjuvant therapy for patients with motor deficits, for example after stroke (Hummel et al., 2005; Adeyemo et al., 2012; Madhavan and Shah, 2012).

Materials and Methods

Ethics Statement

Study protocol and informed consent were approved by the local Ethics Committee for Biomedical Research at the Katholieke Universiteit Leuven, in agreement with the Code of Ethics of the World Medical Association (Declaration of Helsinki) (Rickham, 1964). Written informed consents were obtained from all subjects prior to participation. Financial compensation was given for participation in this study.

Subjects

Thirty healthy subjects (15 females, age 23.9 ± 3.13 years) participated in this study. All participants were right-handed, as assessed by the Oldfield Questionnaire (Oldfield, 1971) (scores 87.73 ± 18.73%). They were naive to the purpose of the study and none had

sensorimotor or neurological deficits (self reported). Each volunteer was screened for risk factors and potential adverse effects caused by transcranial magnetic stimulation (TMS)/tDCS as well as for skin abnormalities at the proposed electrode sites (cut, abrasion, rash) and excluded when necessary. Two subjects dropped out before completion of the study, and one was excluded because of learning gains exceeding more than two standard deviations above the group mean. The remaining 27 subjects (14 in the experimental group and 13 in the control group; 6 females in each group) were included in the statistical analysis. At the beginning of the experiment subjects reported their level of physical activity for the period 2 h prior to the experiment: low, moderate, or high (American College of Sports Medicine, 2006). There were no significant differences in activity levels between groups ($p = 0.82$). An overview of baseline characteristics is given in Table 2.

TABLE 2

Table 2. **Psychometric data**.

Overall Study Design

The present study investigated the effect of applying tDCS, either anodal or sham, to M1 during the acquisition of two different motor tasks: (1) SEQTAP and (2) FORCE. tDCS was applied in a double-blind, sham-controlled design.

Subjects were randomly assigned to an anodal-tDCS or sham-tDCS group. Each group performed two different learning sessions separated by at least 2 months with the order of acquiring the SEQTAP and FORCE task counterbalanced across participants. Stimulation type (anodal versus sham) was kept consistent for each subject in both sessions. Each experimental session consisted of a pre-test (PRE) at day 1, 20 min of motor practice for three consecutive days while either anodal-tDCS or sham-tDCS was applied (Day 1, Day 2, and Day 3), a post-test (POST) 20 min after completion of training on Day 3 and a RT 1 week after the last training session (Figure 1). Instructions, feedback, and motivation were standardized for all sessions. At the beginning of each training session subjects were familiarized with the motor task. Questionnaires using visual analog scales (VAS) (Floel et al., 2004) were performed to evaluate subject's perception of attention and fatigue before and after anodal-tDCS and sham-tDCS sessions. At the end of each session participants were asked to describe their sense of discomfort/pain. Each session lasted between 60 and 90 min.

FIGURE 1
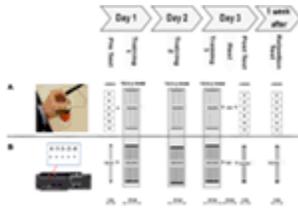
Figure 1. Experimental Protocol. Both motor tasks were acquired following the same systematic order as shown on top of this figure's diagram. **(A)** Modified isometric pinch force task (FORCE) required subjects to control a force sensor with their left thumb and index finger to move a cursor to a series of target zones, as fast and accurately as possible. **(B)** The sequential finger tapping task (SEQTAP) required subjects to repeatedly tap a fixed five element sequence with their left hand, as fast and accurately as possible on a keyboard.

Sequential Finger Tapping Task

Participants were seated on an office-chair approximately fifty centimeters away from a computer screen, with the non-dominant arm performing the task in a supported position. A five-element sequence (4-1-3-2-4) was displayed on the computer screen. Each number indicated a key press with the index (1), middle (2), ring (3), or little finger (4), respectively, which was registered by a computer keyboard (Figure 1B lower panel). Subjects did not receive any feedback regarding performance and the only visual information presented was a black dot appearing underneath each number to indicate that the key press had been recorded (Figure 1B lower panel). Immediately after pressing the last key to complete the five-digit sequence, all dots were removed indicating the start of a new practice sequence. Thus, the visual sequence was permanently displayed on the screen during the entire 40 s practice trial and subjects were instructed to complete as many sequences as they could without a pause. The task was presented with E-prime software (Psychology Software Tools, Inc.). Subjects had to tap the sequence as quickly and accurately as possible for a period of 40 s which was followed by 20 s rest (i.e., task/rest ratio = 2:1). The PRE measurement at baseline consisted of one trial (1 min total). This short duration was chosen because this task is characterized by large initial improvements which might bias PRE performance when included. For the training sessions, 20 trials (20 min) were performed each day. The POST and RT measurements consisted of three trials each (3 min total). All subjects practiced the same sequence throughout all experimental sessions.

Isometric Force Control Task (FORCE)

The FORCE task was slightly modified from a previous version developed by Reis et al. (2009). Subjects were required to control a cursor displayed on a computer monitor with a force transducer using the thumb and index finger of their non-dominant hand (Figure 1A upper panel). They had to move the cursor (green square) between the home position (force = 0) and nine target zones that were visited in a fixed order (6 3 1 7 2 9 5 8 4) (Figure 1A upper panel). The targets were equally distributed over the screen corresponding to 100 virtual units (VU). The size of the cursor corresponded to 5 VU

and the width of each target zone (indicated by two vertical lines) corresponded to 10 VU. The amount of pinch force applied to the sensor was non-linearly related to the displacement of the cursor according to the formula: screen Position = $a \times \ln(\text{force}) + b$ with a and b adjusted such that reaching the furthest target required ~40% of the Maximal Voluntary Contraction (MVC). MVC was taken as the highest value of three maximal pinch force trials at the beginning of the experiment.

The protocol for acquiring the FORCE task was constructed in the same way as the protocol of the SEQTAP task: a PRE measurement at baseline, three consecutive days of training followed by a POST-test (20 min after training at day 3), and a RT after 1 week. For the PRE, POST, and RT measurements, subjects performed the FORCE task while being paced at six different speeds (30, 45, 60, 80, 100, 110 bpm), with a metronome. Each speed was repeated twice in a random order during the pre measurement, and three times for the POST and RT measurements. Subjects were instructed to perform the task as accurately as possible. Again the PRE measurement was shorter than POST and RT measurements to limit the influence of large improvements typically seen at the beginning of learning.

The training session was divided into seven blocks, each block consisting of 2 min performing the FORCE task and 1 min of rest (i.e., task/rest ratio = 2:1), with a total duration of 20 min per session. Training was performed over three consecutive days. Execution speed was chosen by the subject, who was always instructed to perform the task as fast and accurate as possible.

Transcranial Magnetic Stimulation

Transcranial magnetic stimulation was used to localize the hand representation in M1. TMS was delivered via a figure-of-eight coil (70 mm diameter) connected to a Magstim 200 Stimulator (Magstim, Whitland, Dyfed, UK). The coil was positioned over the right hemisphere such that the handle pointed backwards and away from the midline at an angle of 45°. This position ensured a posterior-lateral to anterior-medial flow of the induced current approximately perpendicular to the central sulcus, which is optimal for stimulating the corticospinal pathway of M1. Motor evoked potentials (MEPs) were recorded by an electromyogram (EMG) measured by two disposable Ag-AgCL surface electrodes (Blue sensor SP) placed over the first dorsal interossei (FDI) muscle in a belly-tendon montage and a reference electrode placed over a bone. TMS was used to determine the so-called "hotspot," i.e., the position where MEPs with the highest and most consistent amplitudes were evoked in the left FDI muscle. TMS triggering and EMG recordings were controlled by Signal Software (4.0 Version, Cambridge Electronic Design, UK).

Transcranial Direct Current Stimulation

Transcranial direct current stimulation was applied via two silicone electrodes connected to a battery-driven stimulator (HDCStim class IIa; Model:HDCel EN-05, Newronika s.r.l., Milano 20122, Italy). The active "anode" (5 cm × 5 cm) was covered with an equally distributed amount of conductive gel and located over the FDI hotspot of right M1. The right hemisphere was selected because of the greater possibility of observing further improvements with the less often used non-dominant hand. Since we used a 3-day training protocol performance might plateau too early when the dominant hand would have been used, as observed in the study by Boggio et al. (2006). These authors found a positive effect of anodal-tDCS only when applied to the non-dominant motor area but not to the dominant motor area due to early ceiling effects. The cathodal reference electrode was covered by a sponge (11 cm × 9 cm) soaked in saline solution and positioned on the ipsilateral shoulder. Using a bigger electrode size makes the reference electrode functionally inefficient, due to a spreading of the current, as previously demonstrated by Nitsche et al. (2007). The placement of the cathodal electrode was chosen to prevent additional effects on other areas (e.g., prefrontal cortex) which might be also involved in motor memory formation. Good conductivity of both electrodes was ensured to minimize the risk of burns (Palm et al., 2008) or other skin irritations (Riedel et al., 2012). Placement of each electrode was marked with a waterproof pen to guarantee identical positions during the whole course of the experiment. For anodal-tDCS stimulation a constant current of 1 mA was delivered for 20 min. For sham-tDCS stimulation the same current was applied but only for the first 30 s. All subjects and investigators were blind regarding the tDCS intervention.

Data Analysis

Most motor tasks are affected by the so-called speed-accuracy tradeoff, i.e., accuracy decreases when speed increases and vice versa. A skill index (SI) considers both parameters such that it increases, for example, when movements are performed with the same accuracy but with higher speed or with higher accuracy but the same speed. For the SEQTAP task previous work from our lab indicated that there is a linear relationship between accuracy and speed. Thus the SI for the SEQTAP task was calculated by:

$$SI_{SEQTAP} = \frac{\% \, Correct \, Sequences}{mean \, response \, time \, per \, each \, 40 \, s \, trial}$$

In agreement with Reis et al. (2009), we determined the speed-accuracy tradeoff model of the FORCE task empirically. This was achieved by pacing each subject at different movement frequencies in order to model the associated changes in accuracy. For the FORCE task there was a non-linear relationship between accuracy and speed that is best modeled by:

$$SI_{FORCE} = 1 - \frac{error \, rate}{error \, rate (\frac{1}{n(duration)^b})}$$

In previous work (Reis et al., 2009; Schambra et al., 2011) the b-value was set to b = 5.424, a constant value derived from a small group of subjects performing a control

experiment ([Reis et al., 2009](#)). Here we determined accuracy of the FORCE task for different speeds at PRE, POST, and RT (Figure [2](#)). The POST and RT data were used to determine the "*b*" value for each subject and this value was used to calculate the SI_{FORCE} across all days. On average our value (*b* = 5.14 ± 1.2 SD) was very similar to the value reported previously (*b* = 5.424, [Reis et al., 2009](#)). However, we observed large inter-individual difference across subjects with values ranging from 2.9 to 8.1. Thus, using individually determined *b*-values allows a more accurate reflection of FORCE task performance.

FIGURE 2
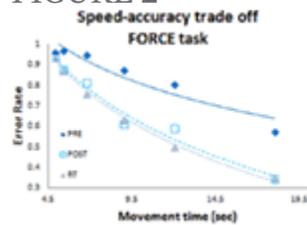
Figure 2. Speed-accuracy tradeoff function. Blue diamonds represent the pre test data set; white squares represent the post test data set; and grey triangles represent the retention data set. Data were included from all subjects (both anodal-tDCS and sham-tDCS groups).

SI_{FORCE} and SI_{SEQTAP} values for each subject were averaged within PRE, POST, and RT sessions, respectively. Changes in SI due to learning gains (online and offline combined) were calculated by subtracting PRE from POST, and long-term retention gains were calculated by subtracting POST from RT. We also calculated the ratio of long-term retention gains relative to the combined learning gains [(RT-POST)/(POST-PRE)].

SI_{FORCE} and SI_{SEQTAP} during training were averaged within blocks. For the FORCE task training there were seven blocks a day. For the SEQTAP task there were 20 trials a day. To compare the training data across tasks, the SEQTAP task data was averaged across three trials (1–3, 4–6, 7–9, and so on) except for the second-last block (averaged over 16–17) to match the seven data points of the FORCE task. Also, since the units of the data differed between tasks, a *z*-transformation was applied.

From the training data we determined the online effects of the FORCE task by subtracting the first trial from the last trial on each day. Offline effects were quantified by subtracting the last trial on 1 day from the first trial of the subsequent day. The same procedure was used for the SEQTAP task, only that the average of the three first and three last trials was used.

Statistics

For analyzing the learning gains (POST-PRE), and the retention gains (RT-POST), non-parametric statistics were used because SI_{FORCE} values deviated from normality, as indicated by Kolmogorov–Smirnov test (*p* > 0.002). Mann–Whitney *U*-tests were used

to identify the stimulation effect by comparing performance gains between the anodal-tDCS and the sham-tDCS group. The within-subjects effect of TASK was analyzed by the non-parametric Friedman's test. Additionally, Spearman correlation coefficients were calculated to compare the gains between tasks.

The training data were normally distributed and an Analysis of Variance for repeated measurements (repeated measures ANOVA) was used with the factors TIME (1–21 SI scores throughout 3-day practice), STIM (anodal-tDCS versus sham-tDCS), and TASK (SEQTAP versus FORCE). Also online and offline gains were normally distributed and subjected to a repeated measures ANOVA with the factors DAY, STIM, and TASK. Paired *t*-tests were used to evaluate the VAS scores of fatigue, attention, and discomfort/pain. The alpha-level was set to alpha = 0.05.

Results
Psychometric Data

Psychometric measurements are summarized in Table 2 for each group and task. Most values are similar across groups and task and the only significant difference between the anodal-tDCS and the sham-tDCS group was found in rating discomfort for the FORCE task: the anodal-tDCS group reported higher values (more discomfort) than the sham-tDCS group. However, overall values were low and this result was not reproduced for the SEQTAP task. Further, subjects were instructed that subjective sensation can vary substantially between subjects and sessions. Therefore, it is expected that subjects of each group were sufficiently blinded regarding the intervention.

Does anodal-tDCS influence SEQTAP learning when comparing PRE, POST, and RT?

Both the anodal-tDCS and sham-tDCS groups improved SEQTAP performance substantially from PRE to POST, while SI_{SEQTAP} remained nearly unchanged from POST to RT (Figure 3A). SI_{SEQTAP}learning gains (POST-PRE) were significantly higher for anodal-tDCS than sham-tDCS ($U = 50$, $Z = 1.96$, $p = 0.04$) while no significant stimulation effects were found for long-term retention (RT-POST) ($U = 73.5$, $Z = −0.82$, $p = 0.41$) (Figure 3B).

FIGURE 3
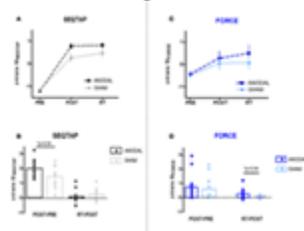
Figure 3. PRE, POST, and RT measurements (upper panel) and learning/retention gains (lower panel). *Z*-transformed data from Skill Index (*z* trans SI) are shown for both tasks. **(A,B)** SEQTAP data: anodal-tDCS (black squares/bars) compared with the sham-tDCS (gray

circles/bars). **(C,D)**FORCE data: anodal-tDCS (blue squares/bars) compared with the sham-tDCS (turquoise circles/bars).

Does anodal-tDCS influence FORCE learning when comparing PRE, POST, and RT?

For the FORCE task, both groups improved from PRE to POST, but additional improvements were observed form POST to RT for the anodal-tDCS group (Figure 3C). Statistics revealed that while SI_{FORCE} gains did not differ significantly during learning (POST-PRE) ($U = 77, Z = 0.65, p = 0.52$), the anodal-tDCS group had significantly larger long-term retention gains (POST-PRE) ($U = 77, Z = 0.65, p = 0.04$) (Figure 3D).

Is the anodal-tDCS effect task-specific?

First we pooled the data across the anodal-tDCS and sham-tDCS groups and tested whether learning or long-term retention gains were correlated between tasks. The Spearman correlation analysis revealed only insignificant effects for both learning ($r = 0.22, p = 0.26$) and long-term retention gains ($r = -0.038, p = 0.85$). This indicates that task learning was largely independent.

As can be seen in Figure 3, learning gains were substantially smaller for the FORCE than the SEQTAP task even after SI values were z-transformed within each task. Therefore we compared the gain-ratios [(RT-POST)/([POST-PRE)] which were smaller for the SEQTAP task than for the FORCE task, but only in the anodal-tDCS group (SEQTAP = 0.05 ± 0.08 FORCE = 0.95 ± 0.46) and not in the sham-tDCS group (SEQTAP = 0.56 ± 0.45 FORCE = 0.073 ± 0.13). Note that small values indicate that gains became mainly expressed during the 3 days of practice rather than due to long-term retention. Friedman's ANOVA revealed a significant main effect of TASK for the anodal-tDCS group [$\chi^2(1) = 7.14, p = 0.007$] but not for the sham-tDCS group [$\chi^2(1) = 0.28, p = 0.59$].

Does anodal-tDCS influence training of each task?

Over the 3 days of practice all subjects improved performance for both SEQTAP and FORCE tasks irrespective of which stimulation was applied (Figures 4A,B). This was further confirmed by a significant main effect of TIME ($F_{20, 500} = 61.3, p < 0.001$). However, over the course of training the anodal-tDCS group improved more strongly than the sham-tDCS group, indicated by a significant TIME × STIM interaction ($F_{20, 500} = 1.85, p = 0.014$). The overall gain was larger for the SEQTAP than for the FORCE task, indicated by a significant TASK × TIME interaction ($F_{20, 500} = 7.24, p < 0.001$). No other main effects or interactions reached significance ($p > 0.11$).

FIGURE 4
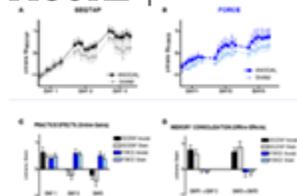
Figure 4. Training Data. *Z*-transformed data from Skill Index (*z* trans SI) are shown for both tasks. **(A)** SEQTAP Training overview for Day 1, Day 2, and Day 3 for anodal-tDCS (black squares) and sham-tDCS (gray circles) **(B)** FORCE training overview for each day between anodal-tDCS (blue squares) and sham-tDCS (turquoise circles) **(C)** Online gains for SEQTAP and FORCE data: anodal-tDCS (black and blue bars respectively) compared with the sham-tDCS (gray and turquoise bars respectively). We determined online effects for the FORCE task by subtracting the first trial from the last trial for each day. For the SEQTAP we used the same procedure, with the only difference that the average of the three first and the three last trials was used. **(D)** Offline effects in the SEQTAP and FORCE data: anodal-tDCS (black and blue bars respectively) compared with the sham-tDCS (gray and turquoise bars respectively). Offline gains in the FORCE task were quantified by subtracting the last trial of 1 day from the first trial of the subsequent day. The same procedure was used for the SEQTAP task, with the only difference that the average of the three first and the last three trials was used. Vertical bars indicate standard errors.

Further analysis revealed that the significant TIME × STIM interaction was mainly driven by the SEQTAP task, which exhibited a significant TIME × STIM interaction when the same repeated measures ANOVA was applied to the SEQTAP data only ($F_{20, 500}$ = 1.88, p = 0.012; Figure 4A). By contrast, performing the same analysis for the FORCE data did not reveal a trend toward a significant TIME × STIM interaction ($F_{20, 500}$ = 0.55, p = 0.944) as shown in Figure 4B.

Did anodal-tDCS influence practice (online effects) versus consolidation (offline effects) differently?

The two tasks differed significantly regarding gains observed due to practice (online effects) and memory consolidation (offline effects): for the SEQTAP task, online gains were only observed for day 1, while the SI_{SEQTAP} scores attenuated during practice at Day 2 and Day 3 (Figure 4C, black/gray bars). Offline-improvements from Day 1 to Day 2, as well as from Day 2 to Day 3 were substantial, as typically expected for this task (Figure 4D, black/gray bars).

By contrast, practicing the FORCE task resulted in robust online improvements for each of the 3 days (Figure 4C, blue/turquoise bars), while offline effects resulted either in unchanged or slightly diminished performance (Figure 4D, blue/turquoise bars).

Accordingly, statistics revealed a significant TASK and TASK × TIME interaction ($F_{20, 500}$ ≥ 16.79, p < 0.001) for the online effects (Figure 4C), and a significant TASK effect ($F_{20, 500}$ ≥ 68.77, p < 0.001) for the offline effects (Figure 4D). However, there were no significant main effects or interactions including the factor STIM.

Discussion

We investigated whether anodal-tDCS effects are task-specific in relation to three different stages of motor skill learning: (i) online effects due to practice, (ii) offline effects due to consolidation, and (iii) long-term retention. Anodal-tDCS over M1 enhanced learning gains (comprising both online and offline effects) for the SEQTAP task, whereas long-term retention was improved for the FORCE task. These findings

confirm our hypothesis that positive effects of anodal-tDCS were present during different learning phases depending on which motor task were acquired.

Our results confirm previous findings that anodal-tDCS is beneficial for motor learning (Nitsche et al., 2003; Boggio et al., 2006; Galea and Celnik, 2009; Reis et al., 2009; Tecchio et al., 2010; Galea et al., 2011; Schambra et al., 2011; Stagg et al., 2011; Kantak et al., 2012; Zimerman et al., 2013). Our most novel result is that the effect of anodal-tDCS is task-specific, with each motor task benefiting from anodal-tDCS at different learning stages. This may suggest that the contribution of M1 to different learning and memory related processes depends on the task acquired.

Why Does Anodal-tDCS Over M1 Influence the Two Tasks Differently?

In the present study we showed that anodal-tDCS over M1 differentially affected learning of the SEQTAP and FORCE tasks: anodal-tDCS facilitated learning gains in the SEQTAP task and long-term retention in the FORCE task. Accordingly, the ratio of long-term retention gains (RT-POST) versus learning gains (POST-PRE) was significantly larger for the FORCE than for the SEQTAP task, but only in the anodal-tDCS group. Consistent with our interpretation, anodal-tDCS facilitated significant performance gains during training only in the SEQTAP task. While the FORCE task also benefited from anodal-tDCS during training, this effect did not reach significance and was not robust across subjects.

For the SEQTAP task it has been argued that distinct brain areas serve different learning stages: according to Doyon et al. (2009), early learning involves predominantly M1 while early consolidation relies strongly on the striatum that supposedly mediates the formation of chunks, an important feature for speeding up tapping performance (Doyon et al., 2009). Based on this model it is not surprising that anodal-tDCS over M1 had little effect on consolidation since the striatum is located underneath the cortex, too deep in the brain to be reached by tDCS. Also, the FORCE task has a sequential element (different targets need to be visited in a fixed order). However, accurate force control is probably the most important sensorimotor parameter determining success. It is well known that M1 neurons play an important role in force control (Ashe, 1997; Keisker et al., 2009;Sulzer et al., 2011). Accordingly, one can hypothesize that not only learning, but also consolidation and long-term retention of improved force control rely predominantly on M1 neurons. Therefore, it is likely that anodal-tDCS over M1 influences all learning mechanisms including consolidation and long-term retention for the FORCE task.

In summary, our findings suggest that anodal-tDCS had a stronger influence on neurons located in M1, i.e., directly underneath the electrodes rather than on more remote areas interconnected with M1, such as the striatum. Therefore, the facilitating effect of anodal-tDCS on motor learning appears to depend on the degree to which M1 is involved in memory formation (Sanes, 2000; Sanes and Donoghue, 2000).

Anodal-tDCS Effect on SEQTAP Task

For the SEQTAP data, anodal-tDCS facilitated memory formation over the course of training. This was indicated by both significantly larger performance gains from PRE to POST and larger improvements during the training sessions from Day 1 to Day 3 for the anodal-tDCS group. However, significance was only reached when online and offline effects were combined since neither measurement reached significance when tested in isolation. This is generally in line with previous work demonstrating beneficial effects of anodal-tDCS on similar sequential tapping tasks. Decreased RT's have previously been observed in subjects receiving anodal-tDCS (Nitsche et al., 2003; Stagg et al., 2011; Kantak et al., 2012). However, in these studies the effect of anodal-tDCS had already emerged during the first practice session, while we observed benefits of the stimulation only after 3 days of training. There are several explanations for these divergent results.

First, the aforementioned studies tested a SRTT, which requires subjects to respond as quickly as possible to a visual cue. An important component of learning in this task is gaining an implicit knowledge of the cued sequence. By contrast, the SEQTAP task requires preprograming and executing a sequence of finger taps as quickly as possible, thereby not relying on external stimuli. Using a paradigm similar to ours, Zimerman et al. (2013) did not find an effect of anodal-tDCS when applied during a 1-day training session in young subjects.

Second, all of these studies placed the cathodal electrode over the contralateral supraorbital area (Nitsche et al., 2003; Stagg et al., 2011; Kantak et al., 2012; Zimerman et al., 2013) while we placed it over the ipsilateral shoulder (as shown in Table 1 and discussed below in further detail). This montage might have resulted in a smaller tDCS effect (Schambra et al., 2011).

Finally, our training protocol required subjects to tap the sequence during continuous 40 s blocks. This might have influenced our SI measure since Brawn et al. (2010) have shown that this form of massed training can cause a phenomenon called reactive inhibition, defined as a decrease in performance due to extensive training. This effect can be observed within trials lasting longer than 10 s. As shown in Figure 4, SI_{SEQTAP} decreased during training on Day 2 and Day 3 which was followed by substantial offline gains when subjects returned the next day. This pattern indicates that reactive

inhibition might have masked true skill performance at the end of training. It is possible that the benefit of anodal-tDCS is derived from a release of reactive inhibition. Note, however, that the POST session was performed 20 min after practice such that effect of reactive inhibition was minimal. Importantly, there were significantly larger gains from PRE to POST for the anodal-tDCS group than for the sham-tDCS group, indicating a real improvement in skill performance.

Anodal-tDCS Effect on FORCE Task

For the FORCE task we found a positive effect of anodal-tDCS on long-term retention only, suggesting that anodal-tDCS had a more robust influence on offline memory formation than on immediate training processes. These findings are partly in line with previous studies using the same task and reporting an overall beneficial effect of anodal-tDCS (Reis et al., 2009; Schambra et al., 2011). However, Reis et al. (2009) reported that anodal-tDCS was most beneficial for offline effects, a result we did not reproduce. In addition to minor differences in the task (we used nine targets as opposed to five), the electrode montage used here was less efficient than that applied by Reis et al. (2009). This argument is further supported by Schambra et al. (2011) who used the same montage as we did and also report a much smaller effect size than (Reis et al., 2009) Reis and Fritsch (2011)(see below for a detailed discussion).

In summary, previous work and our results suggest that anodal-tDCS applied during the FORCE task is mostly beneficial to offline consolidation processes, either over night (Reis et al., 2009) or when testing long-term retention. This proposal is further supported by other work stressing the importance of M1 for motor memory consolidation (Muellbacher et al., 2000; Galea and Celnik, 2009).

Limitations of the Study

Our results are generally in line with previous reports on the beneficial effect of anodal-tDCS over M1 on motor learning, underlining that this technique has great potential, for example, in neurorehabilitation.

However, pinpointing which mechanism might underlie the beneficial effect of anodal-tDCS is difficult because consistency across studies is relatively low. This might be a result of the small sample sizes used here and elsewhere (median n = 12 per group, see Table 1 for an overview) and/or from large inter-individual differences. That is, some volunteers respond strongly to tDCS while others show no effect. First, it is important to note that only some of the applied tDCS current passes through the brain, with as much as half of it being shunted through scalp tissue (Miranda et al., 2006; Sadleir et al., 2010). It has also been suggested that tDCS current might differentially affect neurons based on their orientation and morphology (Radman et al., 2009). Thus, individual

anatomy such as the amount and conductivity of cerebrospinal fluid, the percentage of fat tissue underneath the skin, thickness of the skull, head size, and the orientation of the neurons and gyri at the site underneath the electrode are likely to impact strongly on the response to non-invasive brain stimulation techniques, including anodal-tDCS (Conde et al., 2012; Datta et al., 2012; Truong et al., 2012). This would imply that stimulating all individuals with an intensity of 1 mA is not ideal, because depending on the sample, a large number of non-responders may have contributed to inconsistencies across studies. Therefore, an individualized tDCS protocol utilizing neurophysiological data or computer models would be optimal to test the effects of tDCS and to guide the optimization of clinical trials and electrotherapy.

Another challenge is that stimulation parameters (i.e., intensity and duration) and electrode montage differed substantially across studies (see Table 1) making it difficult to draw general conclusions. Regarding stimulation intensity, Parazzini et al. (2011) showed that the efficacy of tDCS depends on current density since it determines the induced electrical field strength (Parazzini et al., 2011). The current density in our protocol (0.04 mA/cm^2) is very similar to that used previously (Reis et al., 2009; Schambra et al., 2011; Zimerman et al., 2013), and our stimulation duration of 20 min falls within the commonly used range (Reis et al., 2009; Schambra et al., 2011; Zimerman et al., 2013) (see Table 1).

Regarding the tDCS electrode montage, most previous tDCS studies have utilized the contralateral tDCS montage, i.e., with the reference electrode placed on the contralateral supraorbital area. Here we used an extracephalic ipsilateral reference electrode montage (from now on called the ipsilateral montage) that has been shown to enhance focality (Wagner et al., 2007; Datta et al., 2009; Sadleir et al., 2010). The ipsilateral montage has been shown to reliably change the cortical excitability of M1 as measured by TMS (Cogiamanian et al., 2007; Moliadze et al., 2010). However, empirical data suggest that it might be less beneficial for motor skill learning than the contralateral montage (Schambra et al., 2011). This hypothesis was put forward because (i) the effect size of motor learning gains was smaller (Schambra et al., 2011) and (ii) the effect on corticomotor excitability was lower with the ipsilateral compared to the contralateral montage when an intensity of 1 mA was used (Moliadze et al., 2010). However, this line of reasoning has to be considered with care because effect size was compared across studies that investigated different cohorts of subjects and, to the best of our knowledge, no study has demonstrated that larger changes in corticomotor excitability induced by anodal-tDCS are predictive of larger effects on motor learning.

In summary, the lack of multisession tDCS studies makes it difficult to compare our present results to other anodal-tDCS studies that have also targeted M1 to enhance

motor learning. Furthermore, different methodological protocols have been used in the tDCS literature. We stimulated the right hemisphere with 1 mA for 20 min while training by using an ipsilateral montage. In most cases, anodal-tDCS is applied in combination with motor practice, targets the left-hemisphere, stimulates at 1 mA intensity for 15–20 min (current density between 0.02 and 0.04 mA/cm^2) and uses a contralateral montage (for more details, see Table 1).

Nonetheless, the positive effects of anodal-tDCS reported here are in healthy subjects that have an intact motor system. It is possible that when applied to participants with impaired motor systems, e.g., due to aging or neurological disease, this effect might be bigger (Zimerman et al., 2013), providing an optimistic view on the implementation of this technique during rehabilitation.

Conclusion

Our results support the hypothesis that the effect of anodal-tDCS over M1 on motor learning is task-specific. We argue that the nature of the task determines which brain areas contribute to the different processes mediating learning and memory formation. Consequently, anodal-tDCS will preferentially influence processes located in the area underneath the electrode, while effects on remote areas are probably too weak to become functionally relevant.

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgments

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Curing depression and super-charging cranial capacity with deep brain stimulation

By Sebastian Anthony on October 12, 2012 at 10:56 am

Last year, we wrote about a technology called tDCS — transcranial direct current stimulation — that improves your mental acuity by passing a small electrical current through your brain. The US Army and DARPA are already using tDCS to speed up the training of drone pilots and snipers, and one university study even showed tDCS to improve the performance of video game players.

tDCS applies a tiny current (a few volts @ 2mA) to your brain via two electrodes attached to your scalp. Depending on where the electrodes are placed, the current flows through a specific region of your brain, making the neurons more sensitive (i.e. faster-reacting) and increasing their plasticity (better at learning). It really is as simple as it sounds, and you can build your own tDCS equipment very easily. We obviously can't vouch for its safety, but negative side effects seem to be surprisingly rare.

tDCS has a bigger, scarier cousin called deep brain stimulation (DBS). Whereas anyone can build a tDCS "thinking cap," DBS requires the implantation of electrodes within your brain by a very skilled neurosurgeon. These wires then connect to a "brain pacemaker," a which is usually installed under your skin in the chest area. Depending on which region of the brain the electrodes are placed, DBS has proven to be very effective at treating various conditions, such as epilepsy, Parkinson's, and chronic pain. DBS is also being tested as a treatment for major depression, and other affective disorders.

DBS Lead — The lead is a set of thin wires covered with a protective coating. It carries the therapy signal to the electrodes that deliver stimulation to the brain. Approximately 4 inches of the lead are implanted inside the brain. The rest of the lead (about 15 inches) is implanted under the skin of the scalp. Whether a patient has 1 or 2 leads depends upon their medical condition.

Extension — The extension is a set of thin wires covered with a protective coating that connects the lead to the neurostimulator. The extension is connected to the end of the lead, just behind the ear (or where the doctor decides is the best placement). The connection point between the lead and the extension is placed under the scalp. The remaining length of the extension is placed under the skin down the neck to the upper chest area and connects to the neurostimulator. For each lead, there is 1 extension.

Neurostimulator —The neurostimulator contains the power source of the DBS system. The neurostimulator generates and controls the therapy stimulation. The neurostimulator is implanted just under the skin in the upper chest area.

Until now, these brain pacemakers have been "dumb devices," hard-coded to deliver specific electrical pulses for each specific patient. Now, Medtronic, which has been installing DBS systems since 1997, has finally devised a *smart* pacemaker that constantly analyzes your brain activity, then delivers the correct electrical stimulation.

"If you are in the brain already, you might as well take advantage of the fact that you can listen in," Lothar Krinke, manager of Medtronic's DBS division, tells Technology Review. Currently, these DBS systems deliver constant stimulation — even if it isn't needed. With this new system, which measures brain activity, the brain pacemaker will only stimulate the brain when it's needed — Parkinson's suffers, for example, can have symptoms that vary dramatically day to day. This new system will also allow the DBS implant to increase the dosage if the patient's symptoms deteriorate, or turn off entirely at night when stimulation isn't required.
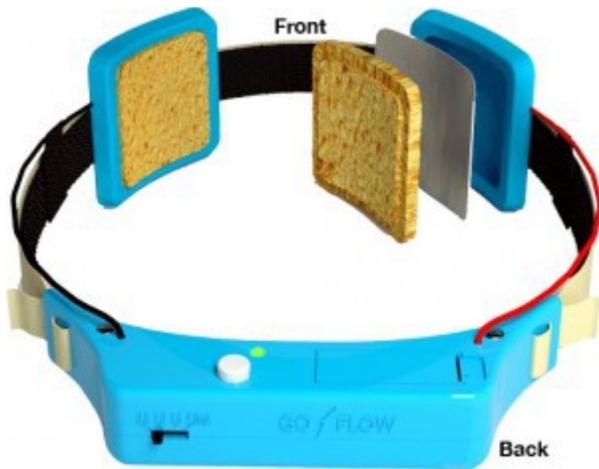
Ultimately, Medtronic's new DBS implant will also act as a fantastic diagnostic tool. Medtronic's researchers will be in the unique position to analyze the brain signals of thousands of patients — which will then feed back into a better understanding of human neurology, and thus even more novel medical solutions. Eventually, we might be able to construct "brain maps" for every brain malady, showing exactly which parts of the brain cause each disorder and disease. The gains for medicine in general, and diagnosticians in specific, would be massive.

And then, of course, there are the *non-medicinal* uses of DBS, which no one is yet to touch upon. If tDCS can halve the time it takes to learn a complex task, I can only imagine the kind of super powers that a correctly-configured DBS system might yield. We are still at the point where we only talk about bionic eyes and prosthetic limbs and DBS as medical procedures — not elective procedures, such as cosmetic surgery. If I *can* install a device that gives me super-human strength or cranial capacity, why shouldn't I?

The New York Times

Jumper Cables for the Mind

Nigel Parry for The New York Times

By DAN HURLEY
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This couldn't possibly be a good idea. On Friday the 13th of September, in an old brick building on 13th Street in Boston's Charlestown neighborhood, a pair of electrodes was attached to my forehead, one over my brain's left prefrontal cortex, the other just above my right eye socket. I was about to undergo transcranial direct-current stimulation, or tDCS, an

experimental technique for delivering extremely low dose electrical stimulation to the brain. Using less than 1 percent of the electrical energy necessary for electroconvulsive therapy, powered by an ordinary nine-volt battery, tDCS has been shown in hundreds of studies to enhance an astonishing, seemingly implausible variety of intellectual, emotional and movement-related brain functions. And its side effects appear limited to a mild tingling at the site of the electrode, sometimes a slight reddening of the skin, very rarely a headache and certainly no seizures or memory loss. Still, I felt more than a bit apprehensive as I prepared to find out if a little bit of juice could amp up my cognitive reserves and make me, in a word, smarter.

Enlarge This Image

Nigel Parry for The New York Times

Dan Hurley sits for a brain-stimulation session.

With the electrodes in place, J. León Morales-Quezada, senior research associate at Harvard's Laboratory of Neuromodulation, pressed a button on his computer and I felt . . . absolutely nothing. No pain. No tingling. Not even a little muscle twitching.

"Is it on?" I asked.

Morales-Quezada assured me it was. For proof, he pointed to a flat-screen on the wall, displaying signals from six electroencephalogram (EEG) monitors also attached to my head.

After 10 minutes of charging my brain, he turned on a computerized exercise I was supposed to practice while the current continued flowing. Called an attention-switching task, it's used by psychologists as a measure of "executive function" or "cognitive control":

the ability to overrule your urges, to ignore distractions and to quickly shift your focus. Young adults generally do better than older people; people with greater overall cognitive abilities generally perform better than those with less.

Scientific papers published in leading peer-reviewed journals since 2005 have shown that tDCS can improve the speed or accuracy with which people perform this attention-switching task. Other studies have found it can improve everything from working memory to long-term memory, math calculations, reading ability, solving difficult problems, piano playing, complex verbal thought, planning, visual memory, the ability to categorize, the capacity for insight, post-stroke paralysis and aphasia, chronic pain and even depression. Effects have been shown to last for weeks or months.

For my attention-switching task, Morales-Quezada explained that if I saw a plus sign on the computer screen, I had to decide whether the number of letters shown immediately after was odd or even, and then press either the "A" key with my left hand, or the "L" key with my right. But if I saw a triangle, he said, I had to decide whether the letters (all of them the same) were vowels or consonants, again by pressing either the "A" or "L" key.

Because I had only a few seconds to respond each time, and because the rule switched back and forth between odd-or-even and vowel-or-consonant, I found my fingers sometimes pressed the wrong key with a seemingly involuntary twitch, even when my conscious mind knew the correct response. It was the same maddening experience many of us have when fooling with our smartphones: meaning to press the camera icon, say, but hitting the calendar instead.

After 20 minutes of stimulation, Morales-Quezada checked my results: I gave 53 correct responses, seven wrong ones, and had an average reaction time of 3.1 seconds. Over five days, I would be stimulated with tDCS for eight 20-minute sessions. If my experience matched those of participants in his studies, I was supposed to either make fewer mistakes, or get faster, significantly more so than if I were not getting stimulated.

The first modern experiments with tDCS came in fits and starts. In 1981, Niels Birbaumer, a neuroscientist at the University of Tübingen, Germany, reported that by applying extremely low doses of direct-current electricity — one-third of a milliamp, not enough to power a hearing aid — to the heads of healthy volunteers, he could speed their response on a simple test of reaction time. The Italian neurophysiologist Alberto Priori began his own experiments in 1992, applying just a tiny bit more electricity, about half a milliamp. He found that enough of the electricity crossed through volunteers' skulls —

electrons flowing from the cathodal electrode to the anodal electrode — to cause brain cells near the anodal to become excited. Despite repeating the experiment multiple times to be sure of the results, it took Priori six years to get his findings published in a scientific journal, in 1998. As he told me, "People kept telling me it can't be true, it's too easy and simple."

One of the first researchers to take Priori's results seriously was Michael A. Nitsche, a clinical neurophysiologist at the University of Göttingen in Germany. "There were two lines of criticism that I heard in those days," Nitsche said. "One line was that it couldn't work, because it's a very weak stimulation and it couldn't get through the cranium. The other was that it should be very dangerous."

In a paper published in 2000, Nitsche showed that the stimulating influence of tDCS lasts for at least five minutes after the electricity stops flowing. In 2003, he reported that the treatment could affect how well a volunteer learns a simple finger movement. Nitsche has followed up with dozens of papers on tDCS.

"I was very skeptical, but Michael Nitsche converted me," said Leonardo G. Cohen, chief of the neurorehabilitation section at the National Institute of Neurological Disorders and Stroke (N.I.N.D.S.) in Bethesda, Md. "It was very difficult for me to accept that simply connecting a battery that you can buy in CVS to electrodes placed on the scalp could change behavior. Then one day I said, I'm going to give it a try."

Cohen and his collaborators enlisted six people who had been partly paralyzed on one side of their bodies for at least one year following a stroke. They found that a single session of tDCS lasting 20 minutes and delivering 1 milliamp to the motor cortex of their brains significantly improved their performance on a standard test of hand dexterity. To be sure it wasn't a placebo effect, they had the participants come in for two sessions, but half were sham treatments in which the electricity came on for only half a minute and then quickly faded off. (Even during active treatment, the feeling of mild tingling that many people experience at the beginning quickly becomes imperceptible, as if the electricity had been switched off.) Although neither the participants nor the experimenters knew whether the treatments were active or sham, the improvement occurred only following the active tDCS. And the benefit was apparent 10 days later.

"The improvements were in the range of only 5 to 10 percent, but an improvement like that after only one application was really very exciting," Cohen said.

Larger, more rigorous studies are now under way to determine the purposes for which tDCS is best suited and the regimen that is most effective — precisely how much electricity, for how long, during how many days, aimed at which brain region — with the hope of eventually winning the approval of the U.S. Food and Drug Administration.

"tDCS will not make you superhuman, but it may allow you to work at your maximum capacity," said Felipe Fregni, the Brazilian physician and neurophysiologist who runs Harvard's Laboratory of Neuromodulation at the Spaulding Rehabilitation Hospital, where I was being treated. "It helps you achieve your personal best level of functioning. Let's say you didn't sleep well the night before. Or perhaps you're depressed, or you suffered a stroke. It helps your brain reach its peak performance."

Fregni and his collaborators at Harvard have published more than 200 papers on tDCS. In 2005, he co-wrote a paper showing that stimulating the left prefrontal cortex while you are doing a particular task can enhance working memory, the ability to track and mentally manipulate multiple objects of attention. He has since tested its effects on migraine, chronic pain, post-stroke paralysis, Parkinson's disease, depression, tinnitus, fibromyalgia, marijuana craving and, strangely enough, the tendency to lie (or, as the paper more delicately put it, "the modulation of untruthful responses").

The evidence, he said, is strongest for depression. Earlier this year he published a study in JAMA Psychiatry involving 120 people suffering from major depression. They received either 50 milligrams per day of the antidepressant Zoloft, 2 milliamps of tDCS, both or a placebo. After six weeks, the mood of those treated with either Zoloft or tDCS alone improved about equally well compared with those in the placebo group. "By itself, tDCS was exactly the same as Zoloft at relieving depression. But when you combine the two, you have a synergistic effect, larger than either alone. That's how I see the effects of tDCS, enhancing something else."

One of the most striking examples of cognitive enhancement comes from research supported by the U.S. Air Force, showing that tDCS improves pilots' vigilance and target detection. "The military has been looking at how to improve vigilance for the past 50 or 60 years," said Andy McKinley, a civilian biomedical engineer who has been studying tDCS at the Air Force Research Laboratory at Wright-Patterson Air Force Base in Ohio. "At minimum we get a twofold improvement in how long a person can maintain performance. We've never seen that with anything else."

But how can a minuscule amount of electricity, applied to the skull for 20 minutes or so, like jumper cables for the brain, make people think better?

I posed that question to Roy Hoshi Hamilton, director of the University of Pennsylvania's Laboratory for Cognition and Neural Stimulation, who has done studies on the effects of tDCS on aphasia, mental flexibility and reading ability. He leaned back in his chair and smiled.

"What is a thought?" he asked. "A thought is what happens when some pattern of firing of neurons has happened in your brain. So if you have a technology that makes it ever so slightly easier for lots and lots of these neurons, these fundamental building blocks of cognition, to be active, to do their thing, then it doesn't seem so far-fetched that such a technology, be it ever so humble, would have an effect on cognition." He went on to explain how the effect could endure. "There's this mantra in neuroscience, coined by Donald Hebb: Neurons that fire together wire together. So I have this tool that makes it more or less likely your neurons will fire. Now, while I'm applying the current, I'm going to have you engage in some behavior, a working-memory task, say, or attempting to name objects even though you have aphasia following a stroke, which is my area of interest. So now that network of neurons is being activated in an environment that slightly nudges it, makes it slightly easier for the neurons to fire and the behaviors to be successfully carried out. Then it's not too far-fetched that, when that happens over and over again, during weeks of practice, those pathways will be reinforced. I agree it does seem very simple. It's not like we're inserting some super-high-tech nanorobots into your brain to clear up cerebral blood vessels. But it is in accord with our thinking about how brains work. And it does appear to have a wide range of effects."

But with some scientists still skeptical, funding from N.I.N.D.S. has not been generous. Daofen Chen, an official at the institute who oversees grants to outside investigators, says: "The question is the scientific premise, the mechanism. They do see some improvement in certain physiological measures. But they are still not able to pinpoint the neurobiological mechanism underlying the recovery. They cannot explain why or exactly how it works for some conditions but not for others." This lack of basic electrophysiological research, Chen explains, is a reason for his institute's modest funding support so far. "The success rate for getting tDCS proposals funded by N.I.H. is less than half the average," Chen says. "That means the peer reviewers" — who make funding recommendations — "are not impressed with the proposals they're seeing in this area."

Or it may mean, in the view of some tDCS researchers, that many scientists simply refuse to believe that a relatively simple, inexpensive technology can work.

"People have come to believe that only complex, expensive medical treatments will be effective," says Vincent Clark, director of the Psychology Clinical Neuroscience Center at the University of New Mexico. The low cost of the technology may seem like an asset, but Clark says it could turn out to be one of the biggest problems in today's medical marketplace.

"Studies are expensive," he says. "There may not be enough money to be made for tDCS manufacturers to be willing to fund the studies required to get it approved by the F.D.A."

But commercial interest is growing, according to Fregni, who is collaborating with a Boston firm on developing a tDCS device that uses ultrasound to target the electrical stimulation deeper into the brain, as a potential treatment for Parkinson's disease. Other firms are developing special electrodes to narrow and limit the current's flow, or to automatically modulate it with EEG monitoring.

"If you had asked me two years ago whether F.D.A. approval for tDCS would ever come, I might have said it would never happen," he told me. "Now companies understand they can add value and get a patent. So now I believe it's feasible."

The chief safety concern of researchers like Fregni is that tDCS is so inexpensive and easy to apply that people will begin treating themselves with homemade devices. In fact, some people have begun to do exactly that: Videos can be found on YouTube showing young men experimenting on their own brains, looking more foolhardy than the cast of "Jackass." What they fail to realize is that applying too much current, for too long, or to the wrong spot on the skull, could be extremely dangerous.

During my eighth tDCS session, on my fifth and final day with Morales-Quezada, my reaction times on the attention-switching task felt considerably faster, and I was now able to consciously override my twitchy fingers' occasional urge to press the wrong key. After looking over the results, Morales-Quezada confirmed my observations. "You made seven errors the first time we tested you," he reminded me, "but during these last four sessions, you made no errors at all. And your reaction time also decreased, from 3.1 seconds to 2.6 seconds today. That's half a second faster, which is extremely good."

Of course, everyone improves with practice, so whether I would have improved just as much if I had never been treated with tDCS is impossible to know. But since hundreds of published studies have shown that the effects of the treatment are real and not the result of

a placebo, it's likely that at least some of my improvement was due to the added effects of the electricity. The benefits are not magical; they still require effort. It's just that tDCS appears to help that effort pay off faster and stronger. Strange? Very. But if the science continues to show that a little zap can safely boost our brainpower, surely some people will find it hard to resist.

Dan Hurley is the author of "Smarter: The New Science of Building Brain Power," which will be published next month by Hudson Street Press.

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