Supporting Information

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SI Methods

Transcranial Direct Current Stimulation. tDCS was applied via 2 flat carbon electrodes covered by a sponge (surface area 25 cm^2 for each electrode) soaked in a saline solution. One electrode was placed over the left motor cortex and 1 electrode was placed on the contralateral supraorbital area (Fig. 2*A*). The anode was centered over M1, at the optimal scalp position for activation of the first dorsal interosseus (FDI) muscle using single suprathreshold transcranial magnetic stimulation (TMS) pulses delivered via a figure of 8-shaped TMS coil (Magstim, Dyfed, United Kingdom). This procedure corresponds reliably to the anatomical position of the hand knob (1). For cathodal tDCS (control experiment), the position of anode and cathode was reversed. In a subgroup of volunteers the accuracy of electrode positioning was additionally determined by coregistration of the subjects' anatomical MRI scan using a neuronavigation device (Nexstim Eximia) (Fig. 2*A*). tDCS was delivered at an intensity of 1 mA (current density 0.04 mA/cm^2; total charge 0.048 C/cm^2) for 20 min in the anodal and cathodal tDCS group and for 30 seconds in the sham tDCS group using a Phoresor II Auto (model PM850, IOMED, Salt Lake City, Utah). The electrical current was always increased in a ramp-like fashion at the onset of the stimulation eliciting a transient tingling sensation on the scalp that disappeared over seconds. At the end of the stimulation, tDCS was ramped down slowly to avoid sensory perception (2). To increase the focality of tDCS we stimulated M1 using smaller electrodes than in previous investigations [25 cm^2 vs. 35 cm^2 (3, 4)]. Subjects and the investigator performing motor testing and data analysis were blinded to the type of intervention.

Sequential Visual Isometric Pinch Task (SVIPT). Subjects were seated in an armchair 60 cm in front of a 20-inch screen monitor. Subjects held a force transducer between thumb and the lateral aspect of the middle phalanx of the index finger of their right hand. Squeezing the force transducer moved a screen cursor horizontally to the right, while relaxing caused the cursor to move left. To increase the difficulty of the task, we chose a logarithmic transduction of pinch force into cursor movement with the maximum rightward movement set to 35−45% of maximum pinch force. Each sequence started upon presentation of a GO signal, while the cursor was in the rest position (HOME). The goal of the task was to move the cursor in a numbered order of gates (Home-1-Home-2-Home-3-Home-4-Home-5), stopping accurately within each gate, returning to the start point, and then moving out to the next gate until finishing at gate 5. A STOP signal appeared when stopping at gate 5. On-screen gate position was numbered 4-1-3-5-2 (left to right). For each of the gates 1–4, subjects had to move the cursor accurately into each gate. If subjects did not enter the gate, we counted an undershoot. If subjects moved the cursor beyond the gate, we counted an overshoot. Both scenarios were judged as an error. Sequence order errors (not following the sequence 1-2-3-4-5) were calculated separately for each trial. Subjects received visual feedback while performing the task. No feedback was given by the investigators.

Psychophysical Assessment. During all sessions, subjects provided information on sleep duration in the previous night, sleep quality, tiredness, attention, general fatigue, hand fatigue of the trained hand, possible discomfort elicited by tDCS, perception of the intensity of tDCS, and potential distraction elicited by tDCS, using questionnaires and visual analogue scales. They also completed the Positive and Negative Affect scale (PANAS) (5), a 20-item self-report measure before and after the training period to screen for possible effects of tDCS on mood. In this assessment negative affect (NA) reflects dispositional dimensions, with high NA epitomized by subjective distress and unpleasant engagement, and low NA by the absence of these feelings. Positive affect (PA) represents the extent to which an individual experiences pleasurable engagement with the environment or again the absence of these feelings. The scores of the questionnaires and ratings (1–10) on the visual analogue scales were averaged per session and stimulation group and subsequently used for comparisons across groups.

Determination of skill

Skill Parameter. The skill parameter method first required characterizing the shape of the SAF. We therefore measured the SAF of the SVIPT before ($n = 12$ naïve subjects) and after 5 days of a 200 trial/day training of the SVIPT ($n = 6$ subjects). Subjects performed 9 blocks of 10 trials each, with each block at a different predetermined movement time. Movement time, representing speed for the SAF, was imposed by a metronome paced at 24, 30, 38, 45, 60, 80, 100, 110, or 120 bpm (each pace required a target hit on the SVIPT). The search for a mathematical model to approximate the SAF was based simply on visualization combined with (*i*) the reasonable constraint that the function is monotonic and (*ii*) the value of only one of its parameters changes appreciably with training. After testing several functions, we came upon a 2-parameter SAF model that satisfied these criteria:

$$\text{error rate} = \frac{1}{1 + a(\ln(\text{duration})^{b})}, \qquad [1]$$

where a and b are the dimensionless free parameters, duration is the average time it took for the subject to complete each trial [i.e., (movement time)$^{-1}$], and error rate is the error rate per block of 10 trials. Error-free blocks were estimated with an error rate of 0.01 to allow the use of logarithmic parameters. Fits of Eq. **1** to SAF data are shown in Fig. 3. While the nonlinear least squares estimate of b changed only −3% with training (from 5.51 to 5.34), the corresponding estimate of a changed 801% (from 0.112 to 1.010). We therefore tentatively defined a as the skill parameter. We planned to then fix the value of b at the value of 5.424 (the average of b pre- and posttraining) and from each bivariate observation of movement time and error rate (averaged over some number of trials), estimate a as:

$$a = \frac{1 - \text{error rate}}{\text{error rate }(\ln(\text{duration})^{b})}, \qquad [2]$$

where a hat indicates an estimator. As we tried a number of possible functions before we settled on Eq. **1**, we were concerned about the possibility of a spuriously good fit, which could mean that using Eq. **2** with a fixed value of b to estimate skill, and ultimately changes in skill with training in both treatment and sham groups, is invalid. We therefore measured the posttraining SAF in a separate validation cohort ($n = 6$ trained subjects). The fit of Eq. **1** to the validation SAF data set was good, which validates the idea that this model is a reasonable approximation to the SAF. The estimate of b from the validation SAF data set was 4.06, which was −24% different from that estimated from the initial SAF data set (5.34). To decide whether this was an important magnitude of difference, we determined the sensitivity with respect to the assumed value of b of the ratio of the estimated a pretraining to the estimated a posttraining (see section on multiplicative change below for an explanation of why a ratio is used). This ratio, which represents an estimate of skill learning, was found to be extremely robust to the assumed value of b, varying $<10\%$ over a range of assumed b values of 1 to 6. This indicates that, for estimating multiplicative changes in the skill parameter a, our method of using Eq. **2** to estimate a with a fixed value of b is acceptably accurate.

Statistical Analysis. All data distributions were tested for normality (Kolmogorov-Smirnov test) before choosing parametrical statistical tests. Group differences were assessed by two-tailed t-test comparisons of baseline performance, total learning, online effects, offline effects retention slope, and skill at day 85 across groups. Bonferroni-Holm adjustment was used, if 2 comparisons were performed. Significance level was set to $P = 0.05$.

Psychophysical Assessment. We did not observe significant differences between the groups in terms of sleep duration in the previous night, sleep quality, tiredness, attention, overall fatigue, hand fatigue of the trained hand, possible discomfort elicited by tDCS, perception of the intensity of tDCS, and potential distraction elicited by tDCS (Table S2). The PANAS scores for PA and NA did not change significantly after training compared to pretraining values.

In addition, there were no significant side effects associated with the stimulation. Mild discomfort, typically described as tingling sensation, at the beginning of the stimulation underneath the tDCS electrodes, was reported in 9 of 12 subjects (75%) in the sham group, 10 of 12 subjects (83%) in the anodal tDCS group, and 10 of 12 subjects (83%) in the cathodal tDCS group. Mild headache was reported in 2 subjects (16.7%) who received sham tDCS and 1 subject who received anodal tDCS (8.3%).

Participants were asked after the experiments whether they received "a real" stimulation or "an inactive" stimulation. None of the groups showed systematic correct awareness of the type of stimulation.

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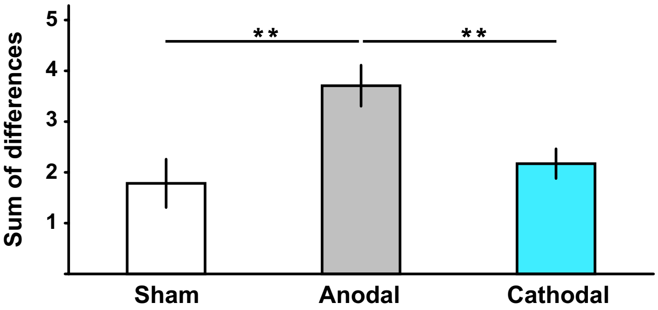

Fig. S1. Polarity-specific effect of tDCS on total learning. Total learning in the sham (white bar), anodal (gray bar), and cathodal (light blue bar) tDCS groups is depicted. Note that total learning with anodal tDCS was superior to either sham or cathodal tDCS (asterisks) and that there were no significant differences between cathodal and sham tDCS, indicating a polarity-specific enhancing effect of tDCS on total learning. Data are presented as mean ± SEM. *, $P < 0.05$; **, $P < 0.01$.

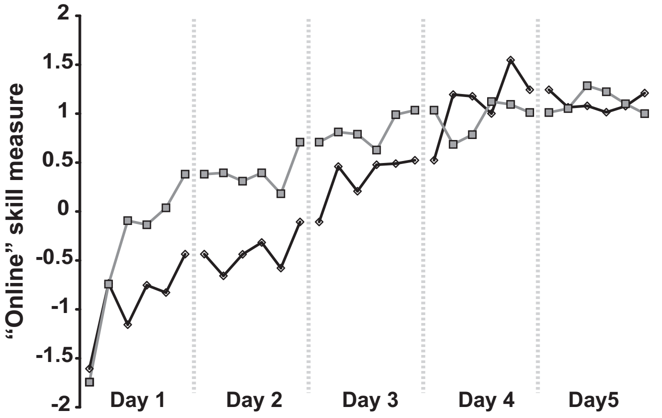

Fig. S2. Time course of online effects. The learning curves for anodal tDCS (gray squares) and sham tDCS (white diamonds) were transformed so that the skill measure of the first block of each day in session $n + 1$ was arbitrarily assigned an absolute value equal to the last block of session n and original values of session $n + 1$ were adjusted to the new value of block 1. In this way, offline effects (dotted lines) are eliminated from the learning curve and only online gains are shown. Note that both groups have reached comparable online gains at day 5 but the anodal tDCS group reaches this maximum earlier at day 3.

Table S1. Participants' demographics: group size, gender, age, training paradigm, and type of tDCS

Stimulation (M1) during training	No. of subjects	Male/female	Mean age	No. of trials/day
Sham tDCS	12	7/5	30.8 ± 3.0	200
Anodal tDCS	12	5/7	28.3 ± 2.2	200
Cathodal tDCS	12	6/6	28.3 ± 1.3	200
Speed–accuracy tradeoff function, pretraining	12	7/5	32.0 ± 3.0	9×10
Speed–accuracy tradeoff function, posttraining	6	3/3	28.3 ± 2.6	9×10
Speed–accuracy tradeoff function, validation	6	2/4	29.0 ± 1.9	9×10

Table S2. Psychophysical data: scores given by the participants using visual analogue scales (0–10) or the PANAS

	Sham tDCS	Anodal tDCS	Cathodal tDCS
Sleep (h)	6.8 ± 0.1	6.7 ± 0.1	7.4 ± 0.1
Tiredness (0–10)	3.0 ± 0.2	3.6 ± 0.2	3.3 ± 0.2
Attention (0–10)	6.7 ± 0.4	7.0 ± 0.2	6.7 ± 0.1
Sequence difficulty (0–10)	3.8 ± 0.4	3.4 ± 0.3	3.7 ± 0.3
tDCS discomfort (0–10)	3.2 ± 0.2	3.5 ± 0.1	2.9 ± 0.1
PANAS positive D1 (10–50)	35.9 ± 2.2	35.4 ± 2.1	33.5 ± 1.6
PANAS positive D8 (10–50)	35.6 ± 1.7	34.7 ± 1.9	33.5 ± 1.7
PANAS negative D1 (10–50)	14.9 ± 1.8	15.1 ± 1.0	14.1 ± 1.0
PANAS negative D8 (10–50)	13.8 ± 1.6	14.0 ± 0.8	14.5 ± 1.2