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Effects of transcranial direct current stimulation of primary somatosensory cortex on vibrotactile detection and discrimination

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Labbé S, Meftah EM, Chapman CE. Effects of transcranial direct current stimulation of primary somatosensory cortex on vibrotactile detection and discrimination. J Neurophysiol 115: 1978–1987, 2016. First published February 10, 2016; doi:10.1152/jn.00506.2015.—Anodal transcranial direct current stimulation (a-tDCS) of primary somatosensory cortex (S1) has been shown to enhance tactile spatial acuity, but there is little information as to the underlying neuronal mechanisms. We examined vibrotactile perception on the distal phalanx of the middle finger before, during, and after contralateral S1 tDCS [a-, cathodal (c)-, and sham (s)-tDCS]. The experiments tested our shift-gain hypothesis, which predicted that a-tDCS would decrease vibrotactile detection and discrimination thresholds (leftward shift of the stimulus-response function with increased gain/slope) relative to s-tDCS, whereas c-tDCS would have the opposite effects (relative to s-tDCS). The results showed that weak a-tDCS (1 mA, 20 min) led to a reduction in both vibrotactile detection and discrimination thresholds to 73–76% of baseline during the application of the stimulation in subjects categorized as responders. These effects persisted after the end of a-tDCS but were absent 30 min later. Most, but not all, subjects showed a decrease in threshold (8/12 for detection; 9/12 for discrimination). Intersubject variability was explained by a ceiling effect in the discrimination task. c-tDCS had no significant effect on either detection or discrimination threshold. Taken together, our results supported our shift-gain hypothesis for a-tDCS but not c-tDCS. transcranial direct current stimulation; psychophysics; somatosensory cortex; cortical plasticity; tactile; vibration

One form of noninvasive brain stimulation is transcranial direct current stimulation (tDCS), whereby weak direct current is applied over a cortical region, using large surface-area electrodes to modify cortical excitability. Depending on the polarity of the current, tDCS is thought to increase [anodal (a)-tDCS] or decrease [cathodal (c)-tDCS] cortical excitability (Nitsche and Paulus 2000). The effects can, moreover, outlast the period of stimulation, up to 90 min after a single session of tDCS (Nitsche and Paulus 2001). With repeated sessions of tDCS, Reis et al. (2009) showed that enhanced motor performance can persist for up to 3 mo. Mixed results have, however, been reported. For example, Wietzhoff et al. (2014) recently reported large differences among subjects, with only one-half of their subjects showing evidence of increased cortical excitability after a-tDCS over primary motor cortex (M1). In addition, close to one-third of their subjects showed the same sign of effect for opposite polarities of stimulation, facilitation with both a- and c-tDCS.

There is currently a lot of interest in this technique and particularly its potential to induce long-lasting cortical plasticity in various clinical applications, such as motor rehabilitation poststroke and treatment of conditions ranging from chronic pain to depression (Kuo et al. 2014; Plow et al. 2012; Schlaug et al. 2008). The underlying mechanisms have yet to be fully determined, but it has been suggested that the long-term effects may involve activity-dependent release of brain-derived neurotrophic factor (BDNF) (Fritsch et al. 2010). The synaptic mechanisms may involve the induction of long-term potentiation and/or depression [reviewed in Dayan et al. (2013)].

Little is known about the effects of tDCS applied to primary sensory areas on either cortical excitability or perception. One of the pioneering studies was that of Antal et al. (2003), who reported that tDCS over visual cortex produced polarity-dependent changes in the threshold for eliciting phosphene by transcranial magnetic stimulation (TMS) applied to visual cortex: a-tDCS lowered the threshold, whereas c-tDCS raised the threshold. Recently, enhanced auditory discrimination has been reported with a-tDCS over auditory cortex (Impey and Knott 2015). Only a handful of studies has investigated the effects of tDCS over primary somatosensory cortex (S1), and the results, to date, are mixed. Ragert et al. (2008) and more recently, Fujimoto et al. (2014) reported that tactile spatial acuity [grating orientation test of Van Boven and Johnson (1994) on the finger is improved during and after a-tDCS to contralateral S1. In contrast, Grundmann et al. (2011) reported no change in touch threshold with either a- or c-tDCS polarity, possibly reflecting the lack of sensory testing during tDCS. Changes in cortical excitability should be reflected by changes in the amplitude of somatosensory-evoked potentials (SEPs). Dieckhofer et al. (2006) reported a trend (nonsignificant) for increased SEPs with a-tDCS to S1, whereas c-tDCS had the opposite effect, a long-lasting, significant decrease in N20 (presumed to originate in area 3b). To summarize, there is no consensus, at present, as to whether or how S1 tDCS modulates tactile perception and S1 cortical excitability.
The purpose of this study was to examine tactile perception before, during, and after S1 tDCS with the goal of determining the effects of tDCS on tactile perception and also gaining insight into the underlying neuronal mechanisms. Our general hypothesis was that tactile perception would improve with a-tDCS compared with sham (s)-tDCS and decline with c-tDCS, again compared with s-tDCS. With the use of the same tDCS protocol as Ragert et al. (2008), we examined performance on two tactile tasks: vibration detection and vibration amplitude discrimination. This choice of tasks allowed us to test what we call the shift-gain hypothesis, illustrated in Fig. 1, inspired by our previous work examining the perceptual consequences of movement-related gating on tactile perception (Chapman et al. 1987). The rationale for this hypothesis is based on proposed changes in the origin and slope of the theoretical stimulus-response curve plotted in Fig. 1. The origin corresponds to the minimal perceived stimulus intensity, detection threshold. If cortical excitability is increased (a-tDCS), then subjects will be able to detect weaker stimuli (reduced detection threshold), reflecting a shift to the left of the stimulus-response function. A decrease in cortical excitability (c-tDCS) will have the opposite effect, a shift to the right (higher detection threshold). Discrimination threshold, in contrast, measures the just-noticeable difference between pairs of supraliminal stimuli, providing information on the slope or gain of the underlying stimulus-response function. Thus a decrease in discrimination threshold (improved performance) would reflect an increase in the slope of the curve; an increase in discrimination threshold would reflect a decrease in slope. With these two measures, we can therefore determine how tDCS modifies tactile perception and infer changes in cortical excitability. The only type of mechanical stimulus that has sufficient precision to evaluate both sensory abilities is vibrotactile stimulation, a method used extensively to study the neuronal mechanisms underlying tactile perception (Mountcastle et al. 1972, 1980; Romo and de Lafuente 2013; Romo et al. 2012).

The results have been presented in abstract form (Labbé et al. 2014).

**METHODS**

**Subjects**

For the detection task, a total of 13 healthy, naïve participants, all right handed (self-declaration: hand used for writing), were recruited: 9 women and 4 men, ages 18–25 yr (mean, 22 yr). For the discrimination task, 12 subjects were recruited, 6 women and 6 men (3 left handed; mean age, 23 yr; range, 19–30 yr). Three subjects participated in both tasks. For each task, the subjects participated in three experimental sessions, 2 h duration each, in which the effects of a-, c-, and s-tDCS on the task were examined. For the detection task, sessions were separated by 1 wk (Ragert et al. 2008); this was reduced to 3 days for the discrimination task (Fujimoto et al. 2014; Weithoff et al. 2014). The experimental protocols were approved by the Institutional Ethics Committee, and all subjects gave their written, informed consent before participating. The subjects were remunerated for their participation.

**Vibrotactile Stimuli**

The test stimuli consisted of 20 Hz sinusoidal vibration delivered by a lever arm, to which a 3.1-mm diameter nylon sphere was affixed (see Fig. 2B). Lever arm displacements (1 μm resolution) were generated by a servo-controlled direct current motor (Model 305B dual-mode lever arm system; Aurora Scientific, Aurora, ON, Canada) that was, in turn, controlled by custom-written software. The motor and lever arm were mounted on a heavy steel plate affixed to a table.
Experimental Setup

During the experiment, participants were comfortably seated in a chair with the arm resting on a second independent table (forearm pronated; Fig. 2A). The hand rested on a small plaque, with a 2 × 2-cm opening that extended beyond the table. The tip of the left middle finger (D3) was positioned in the center of the opening. Before the start of stimulation and data acquisition, the lever arm of the vibrator was adjusted so that the nylon sphere just contacted the center of the distal phalanx of D3 (Fig. 2B). Before testing, a 0.5-mm preindentation of the skin was applied.

Tactile Detection Task

The events in a sample trial in the detection task are shown in Fig. 3A. Each trial began with a 200-ms warning tone (1,000 Hz); 500 ms later, a second tone (120 Hz, 1 s) occurred. This signaled the 1-s observation period. In 50% of trials (signal), there was 20 Hz vibration present (duration, 1 s); the other trials (nonsignal) had no vibration. Three amplitudes of vibration were presented in each block of trials: one was subthreshold, one corresponded to the threshold estimated at the beginning of the session (see below), and the third was suprathreshold. After the tone ended, the subject verbally reported whether the stimulus was present or absent and rated his/her confidence in this decision using a five-point scale (1 = certain that signal was absent; 2 = rather certain that signal was absent; 3 = unsure whether signal was present or absent; 4 = rather certain that signal was present; 5 = certain that signal was present). The response was entered in the data file by the experimenter. Immediately after, the next trial began.

There were 120 trials in each test block: 60 signal trials (3 amplitudes × 20 trials) and 60 nonsignal trials. The order of trials was quasirandom. Each block took ~10 min. At the beginning of the session, we presented several large-amplitude stimuli (>15 μm) to the subjects to familiarize them with the vibrotactile sensation. Thereafter, the rating scale was presented, along with instructions to use the entire scale and to stay immobile during testing. Subjects were informed that different amplitudes of vibration would be presented, including some very small vibrations, and that some trials would have no vibration. The detection threshold was then estimated using up and down staircases (yes-no paradigm), starting from an initial amplitude of 15 μm. From this, three amplitudes of vibration were chosen for the formal testing: estimated threshold plus one above and one below. In most cases, amplitudes of 2, 6, and 10 μm were used (range, 1–14 μm). Subjects then executed a block of practice trials; knowledge of results was provided at this time. If necessary, the choice of amplitudes was adjusted. The number of practice trials varied (40–60); testing continued until the subject’s performance was stable. During the formal testing, no feedback on performance was provided.

Tactile Discrimination Task

A two-alternative, forced-choice paradigm was used. Subjects were presented with pairs of stimuli (duration, 800 ms) and asked to identify which was stronger by clicking on the corresponding button of a mouse. As shown in Fig. 3A, each trial in the discrimination task began with a 120-Hz tone (present throughout the trial). After a delay (700 ms), the first 800-ms stimulus was presented. The second stimulus was presented 800 ms later. The response window (duration, 2.8 s) began at the onset of stimulus 2. Each pair of stimuli consisted of a standard stimulus (50 μm amplitude) and a comparison stimulus (variable amplitude: 50, 53, 56, and 59 μm, corresponding to differences of 0, 3, 6, and 9 μm). The subjects were naïve with regard to the presence of 20 identical trials. The order was counterbalanced. Subjects were encouraged to respond as quickly as possible. The next trial began after the end of the response window.

There were 80 trials in each block; 20 trials for each comparison amplitude. Each block took ~8 min. To familiarize the subject with the task at the beginning of the session, five trials were first presented with large differences of 20, 25, and 30 μm; then, five other trials were presented with smaller differences: 5, 10, and 15 μm. Feedback was provided after each trial. This was followed by a training block of 40 trials using the formal test amplitudes of 50 (standard), 53, 56, and 59 μm. Thereafter, data acquisition began. As for the detection task, no feedback on performance was provided during the formal testing.

Transcranial Direct Current Stimulation

In these experiments, subjects were blind as to the type of stimulation. The order of testing across sessions was completely counter-
balanced (e.g., 4 subjects started with a-tDCS; 4 with c-tDCS, and 4 with s-tDCS, etc.). For electrode placement, a 10–20 EEG helmet was placed on a participant’s head at the beginning of the session. The active electrode, anode or cathode, was centered over the right S1 cortex (C4’); the indifferent was placed over the left orbit (Fig. 2A). To diminish resistance, the skin at the site of the electrodes was first vigorously cleansed with alcohol. Electrodes (4.2 × 4.5 cm) were inserted into 5 × 5 cm saline-soaked sponges, and two elastic bands were used to fix them in place; tDCS was delivered by a battery-driven tDCS low-intensity stimulator (Model 1300A; Soterix Medical, New York, NY). For the active conditions, a- or c-tDCS was applied for 20 min at 1 mA (0.04 mA/cm²) with current ramped up at the beginning and the end over 30 s. Current delivery was monitored throughout the testing. For the sham condition, the current was gradually ramped up to 1 mA over 30 s and then decreased to 0 (anode over S1). The same up and down ramp occurred at the end of the 20 min of sham stimulation.

**Experimental Design**

For both tasks, there were five blocks of trials in each session (Fig. 3B): two blocks before tDCS (pre1 and pre2), one block during tDCS, and two blocks after tDCS (post1, post2). Testing before and after tDCS was separated by 20 min, with the tDCS beginning immediately after the pre2 block. Testing during tDCS began 5 min after the onset of stimulation for the detection task and 6 min for the discrimination task. During the pauses, the subject remained seated but was allowed to remove his/her hand from the table. The site of stimulation on D3 was marked so that the lever could be repositioned accurately. Trials in which the subject moved or was distracted were excluded and repeated at the end of the block of trials. At the end of each session, the subjects were asked to rate their degree of discomfort associated with tDCS and the intensity of the perceived sensation evoked by the tDCS stimulation using a numerical scale, ranging from 0 (no discomfort, no sensation) to 10 (intolerable or very strong).

**Data Acquisition and Analysis**

For the detection task, a total of 1,800 trials was recorded for each subject; 600 trials/session. For each trial, contact force was recorded (1 kHz), along with the subject’s response. The force signals were individually inspected using custom software (Matlab version 2013b; MathWorks, Natick, MA). In the initial analyses, we generated receiver operating characteristic (ROC) curves by plotting the hit rate (HR; proportion of signal trials correctly identified) as a function of the false alarm rate (FAR; proportion of nonsignal trials incorrectly identified as signal trials) for each of the three amplitudes presented and calculated the sensitivity index (d’). The d’ values for the three amplitudes were, as planned, distributed around threshold (d’ = 1.35), corresponding to 75% correct detection [halfway between chance (50%) and perfect performance (100%)]. The d’ values were plotted as a function of amplitude, and from this, threshold was interpolated. However, in several cases, the lowest amplitude generated a negative d’, which led to an overestimation of the threshold. To avoid this problem, we used a nonparametric measure of detection threshold for all data, the area under the ROC curve that was calculated for each amplitude of stimulation (Brown Grier 1971). Area was plotted as a function of amplitude, and threshold (0.75) was interpolated. When all of the d’ values were positive, the two measures gave closely similar estimates of threshold. We also calculated the criterion (C; response bias) for each subject in each block of trials: C = -0.5(zHR + zFAR) (Macmillan and Creelman 1990).

For the discrimination task, the response, contact force, and reaction time (RT; measured from the onset of stimulus 2) were recorded in a total of 1,200 trials for each subject (400 trials/session). In every block of trials, the proportion of correct responses was calculated for each of the three comparison stimuli. These three values were plotted as a function of the change in amplitude, and from this, threshold was interpolated (proportion correct = 0.75).

Statistical analyses of the data were performed using repeated-measures (RM) ANOVA and post hoc comparisons (Tukey least significant difference with a Bonferroni correction). These analyses first established that baseline estimates of threshold (pre1, pre2) were stable within and across the three sessions so that data could be normalized (percent baseline for each session). As described in RESULTS, the main effect seen here was a modest decrease in threshold during a-tDCS, but not all subjects showed a decrease. We initially examined the percent change in threshold relative to baseline. Subjects were categorized as responders if there was a 10% or greater decrease in threshold during and/or immediately after a-tDCS. This subjective categorization was then confirmed by applying a k-means cluster analysis to the data from the anodal sessions (all 5 blocks), since this is the polarity that had consistent effects here. The group number was set to two (threshold could decrease or not), and a Euclidian distance metric was applied. Subsequently, the data from each session (a-, c-, and s-tDCS; all 5 blocks) were analyzed using an RM ANOVA (threshold/block; factor, a-group membership) and the results used to calculate the effect size, the partial η², as follows

\[\eta^2_{partial} = \frac{SS_{group}}{SS_{group} + SS_{error}}\]

This analysis, where SS is sum of squares, allowed us to determine whether subjects identified as responders during a-tDCS reacted in the other sessions (c- and s-tDCS) in any common fashion. For the anodal responders, the main analysis then evaluated the effects of tDCS (3 conditions) on threshold across the five test blocks. When a significant change was identified across the three sessions, then post hoc comparisons were performed (a- vs. s-tDCS; c- vs. s-tDCS). Similar analyses were applied to other measures, including the FAR (detection) and the subjective estimates (discomfort, intensity of tDCS).

Note that when data were not normally distributed (Shapiro-Wilk test), and/or variance was not homogeneous (Levene’s test), then the nonparametric equivalent, Friedman test, was used. All analyses used Systat, V11.0 (SPSS, IBM, Armonk, NY). The level of significance was fixed at P ≤ 0.05 for all analyses.

**RESULTS**

**Vibrotactile Detection Task**

**Baseline measures.** Median contact force across all subjects and all trials was 0.032 N (25–75%, 0.016–0.046 N). There was no significant difference between the signal and nonsignal

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*Subject 1 detected the smallest amplitude that the vibrator could generate.

We assigned a default value of 1 μm. pre1/2. 2 trial blocks before transcranial direct current stimulation.

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trials ($P = 0.83$, Kruskal-Wallis test). Table 1 summarizes the baseline vibrotactile detection thresholds (blocks pre1 and pre2) for all subjects. Mean threshold (frequency of 20 Hz) was 4.4 ± 0.1 μm. There was little change in threshold from one session to the next: 4.4, 4.6, and 4.3 μm for sessions 1, 2, and 3, respectively. This was confirmed using an RM ANOVA (dependent variable, threshold; factors: session, $P = 0.22$; block, $P = 0.36$). However, as illustrated in Table 1, the threshold varied considerably among subjects (range, 2.1–7 μm). To pool the data, we therefore expressed the threshold values as a percentage of the individual control threshold for each session.

Overall, the subjects correctly identified 62% of the stimuli presented (2,885/4,680) during the baseline testing. The mean HR during the baseline testing was similar across the three sessions: anodal session, 60%; cathodal, 64%; and sham, 61%. One subject was an outlier, detecting up to 96% of the stimuli (subject #1, Table 1). Threshold could not be estimated for this subject ($<1 \mu$m, corresponding to the smallest amplitude that could be delivered). The data from this subject were therefore excluded from further analyses.

There were few false alarms during the baseline testing (anodal session, 6.9%; cathodal, 7.5%; and sham, 6%), and the FAR was stable across sessions ($P = 0.38$). This observation was extended to all testing (3 conditions; 5 blocks of trials), with both factors insignificant ($P = 0.68$ and $P = 0.19$, respectively). Such an observation suggests that subjects kept the same C across sessions. Consistent with this, C showed no significant change during the baseline testing, either across the three sessions ($P = 0.28$) or the two testing blocks ($P = 0.17$). These observations were extended to include all testing (3 conditions; 5 blocks of trials): there was no change in C, either across sessions ($P = 0.27$) or blocks ($P = 0.89$).

**Effects of tDCS.** The effects of a-, c-, and s-tDCS on tactile detection were assessed in 12 subjects. All subjects reported a painless itching sensation at the onset of tDCS under each electrode. No other side effects were reported either immediately after the session or 24 h later. The levels of discomfort [median, 2 (25–75%, 1–3); maximum score, 10] and the reported intensity of the tDCS [median, 4 (25–75%, 3–5); maximum score, 10] were similar across the three sessions ($P = 0.22$ and $P = 0.66$, respectively, Friedman test).

Wiethoff et al. (2014) recently reported a large degree of variability across subjects when examining the effects of M1 tDCS. For this reason, we initially examined the results of each subject to identify trends in the observed effects. The individual data from six representative subjects are plotted in Fig. 4A. Shown are three subjects with improved detection (decreased threshold) during a-tDCS and data from three (of 4) subjects with no improvement during a-tDCS. The majority of subjects (8/12) showed a decrease in threshold during a-tDCS, but this did not persist after the end of a-tDCS for all subjects [subject 9 (S9)]. There was little evidence for opposite effects during c-tDCS: one subject (S13) showed a modest increase in threshold to 110–112% of baseline during and after c-tDCS. The other subject (S11) showed a larger increase to 122% during c-tDCS, but this was followed by a prolonged decrease to 75–78%. Finally, both polarities of tDCS had the same effect for S9. Altogether, no obvious trends could be identified for c-tDCS, with only three subjects showing some evidence of opposite effects during tDCS. With s-tDCS, in contrast, there was a general trend for increased thresholds after s-tDCS. Overall, 8 of 12 subjects showed a decrease in threshold during a-tDCS of ≈10%, an observation that was confirmed with a k-means cluster analysis applied to the a-tDCS data. The separation was, however, restricted to two test blocks—during a-tDCS and post1 (large F values). This was confirmed with post hoc tests (see below). Figure 4B plots the results of the anodal responders and nonresponders separately during the a-, s-, and c-tDCS sessions. The separation during and immediately after a-tDCS is clearly evident (Fig. 4B). For the responders, threshold decreased to 73% of control during a-tDCS. Threshold was still reduced in the first block of testing after a-tDCS (92%) but recovered to the control level (104%), 30 min after a-tDCS. The data from the cathodal session (Fig. 4B), in contrast, show that neither group (anodal responders vs. nonresponders) showed a change in threshold during c-tDCS. Finally, both groups showed an increase in detection threshold after s-tDCS (anodal responders, 125%; nonresponders, 144%; Fig. 4B).

An RM ANOVA (threshold/block) across the five blocks of the anodal session confirmed that threshold varied significantly as a function of group ($P = 0.001$) and block ($P = 0.021$). Group membership explained 71% of the variance in detection threshold (median effect size; block, 24%). The difference across the responders and nonresponders was independent of both their baseline threshold (4.7 ± 0.4 and 4.8 ± 0.8 μm, respectively; $P = 0.73$) and C ($P = 0.32$). An RM ANOVA applied to the data from the cathodal session showed that there was no difference in threshold, either as a function of group (anodal responders vs. nonresponders; $P = 0.33$) or block ($P = 0.32$). In contrast, the data from the sham sessions showed a significant change across blocks ($P = 0.004$; effect size, 82%) but not group. The former likely reflected the trend for higher thresholds that were observed with repeated testing.

To examine the effects of tDCS across the three sessions, an RM ANOVA analysis was applied to the data of the anodal responders (threshold/tDCS, ×3; block, ×5). Both factors were significant (tDCS, $P = 0.013$; block, $P = 0.013$), with modest effect sizes (46% and 35%). Post hoc tests showed that there was a significant difference between the a- and s-tDCS sessions ($P = 0.011$; effect size, 63%) but not between the c- and s-tDCS sessions ($P = 0.199$; effect size, 22%). The significant differences (a- vs. s-tDCS) were, moreover, limited to two blocks of trials (Fig. 4B), during ($P = 0.049$; effect size, 45%) and immediately after ($P = 0.02$; effect size, 56%) tDCS. Finally, we examined the data to determine if the magnitude of the observed decrease in threshold with a-tDCS covaried with the baseline threshold. No evidence of a significant relationship (regression) was found during or immediately after a-tDCS ($P > 0.2$).

**Vibrotactile Discrimination Task**

**Baseline measures.** Median contact force across all subjects and all trials was 0.046 N (25–75%, 0.034–0.06 N). There was no significant difference across the two observation intervals ($P = 0.75$, Kruskal-Wallis test). Overall, subjects correctly identified the larger stimulus in 75.5% of the trials that contained a change in amplitude (8,151/10,800 trials). This result suggests that the chosen amplitudes were, as planned, distributed around threshold (75% correct). Table 2 summarizes the mean baseline vibrotactile discrimination thresholds (blocks...
pre1 and pre2) for 12 subjects in each of the 3 experimental sessions. Mean discrimination threshold was $7.5 \pm 0.4 \mu m$ (standard amplitude, 50 $\mu m$). There was little change in mean threshold across sessions 1, 2, and 3: 8, 7.2, and 7.4 $\mu m$, respectively. This impression was confirmed with an RM ANOVA (dependent variable, threshold; factors: session, $P = 0.25$; block, $P = 1.0$). As found for the detection task, there was considerable variability among subjects (range, 3–13.5 $\mu m$), and so we expressed the threshold values as a percentage of the mean baseline threshold for the session to pool the data.

**Effects of tDCS.** The sensation elicited by tDCS was as described above. In this series, two subjects reported side effects after one session: a frontal headache that appeared 24 h after the cathodal session and fatigue after the cathodal session (onset, 3 h after the session in the morning; duration, until bedtime). As for the detection task, there were no significant differences across sessions regarding the levels of either discomfort [median, 2 (25–75%, 1–3); $P = 0.43$, Friedman test] or the perceived intensity of the tDCS [median, 3.5 (25–75%, 1.5–5); $P = 0.24$].

Vibrotactile discrimination threshold was estimated before, during, and after a-, c-, and s-tDCS. As for the detection testing, we first examined the results of each subject to identify trends in the data using a change of 10% in the threshold (increase or decrease), during and/or immediately after tDCS, as our criterion. Once again, only a-tDCS appeared to have a significant effect on vibrotactile perception.

**Table 2.** Mean baseline vibrotactile discrimination thresholds ($\mu m$) in 12 subjects (blocks pre1 and pre2; frequency, 20 Hz)

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**Fig. 4.** Detection (De) task. A: individual results from 6 representative subjects (S) for the a (filled circles)-, s (open circles)- and c (triangles)-tDCS sessions. Threshold (percent of baseline) is plotted as a function of time. tDCS was applied for 20 min (shaded bars). Subjects were categorized according to the changes seen during a-tDCS (cluster analysis, see text): 8 of 12 subjects showed a decrease in detection threshold during a-tDCS, anodal responders (3 examples, top). The remaining subjects (3 examples, bottom) were categorized as anodal nonresponders. No consistent patterns were observed for c-tDCS or s-tDCS. B: pooled data (means ± SE for the anodal responders) from all subjects plotted as a function of whether they were categorized as responders (filled squares) or nonresponders (open squares) during a-tDCS. No SE for the nonresponders ($n = 4$). *Significant differences (a- vs. s-tDCS) are indicated (see text).
consistent effects. Figure 5A shows examples of three subjects who showed a decrease in threshold during a-tDCS and three subjects without a decrease. The anodal responders all showed a modest decrease during a-tDCS, followed by a larger decrease in the first block of trials post-tDCS. These subjects were typical in that c-tDCS did not have the opposite effect: two subjects showed a decrease in threshold during c-tDCS, and the other showed no change. Variable results were obtained in the anodal nonresponders during the anodal session (no change and an increase; Fig. 5A). Overall, 9/12 subjects were categorized as anodal responders. This classification was confirmed with a cluster analysis that showed large separations during and immediately after a-tDCS (large F values). This separation was confirmed with post hoc tests (see below).

Figure 5B plots the pooled results from the anodal responders and nonresponders from each session. During a-tDCS, threshold decreased to 76% in the responders; a further decrease to 53% of baseline was obtained immediately after a-tDCS. Twenty minutes later, threshold was close to baseline. In contrast, the nonresponders showed evidence of an increase in threshold during and after a-tDCS. During c-tDCS, the anodal responders showed a decrease in discrimination threshold during and after c-tDCS, to 80–90% of baseline. In contrast to the results obtained with the detection task, neither group of subjects showed evidence of an increase in threshold with s-tDCS.

An RM ANOVA, across the five blocks of the anodal session, confirmed that threshold varied significantly as a function of group ($P = 0.008$) and that this factor explained 52% of the variance in discrimination threshold. Block was not significant, but there was a significant interaction (group × block, $P = 0.011$; effect size, 27%). In contrast, neither group nor block was a significant factor for the other two test conditions, s- and c-tDCS, despite the small decrease during c-tDCS. The effect sizes (group) were correspondingly small (3.2% and 1.9%, respectively). A final RM ANOVA compared performance across the three tDCS sessions in the subjects categorized as anodal responders (threshold/tDCS, $H = 3$; block, $H = 5$). Threshold showed significant changes both as a function of tDCS ($P = 0.015$; effect size, 41%) and block ($P = 0.045$; effect size, 36%). As found for detection threshold testing, there was a significant difference between the anodal and sham sessions ($P = 0.005$; effect size, 64%) but not between the cathodal and sham sessions ($P = 0.094$; effect size, 31%). Post

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**Fig. 5.** Discrimination (Di) task. A: individual results from 6 representative subjects (plotted as in Fig. 4): a-tDCS responders (top; decreased threshold) and nonresponders (bottom). The 3 responders were also tested in the detection task several months earlier (same subjects shown in Fig. 4A; top; note that the subject numbers differ: De-S9 = Di-S11, etc.). All 3 showed improved tactile detection and discrimination during a-tDCS (decreased threshold). As for the detection task, most subjects ($n = 9$) showed a decrease in detection threshold during and/or after a-tDCS; 3 of 12 showed either no change (bottom left) or an increase (bottom middle and right) during a-tDCS. Some of the former also showed a decrease during c-tDCS (e.g., Di-S11). B: pooled data from all subjects as a function of their categorization as a-tDCS responders or nonresponders. Plotted as in Fig. 4B. *Significant differences (a- vs. s-tDCS) are indicated (see text).
hoc tests likewise revealed that the significant difference (a- vs. s-tDCS) was limited to the testing during ($P = 0.006$; effect size, 64%) and immediately after ($P < 0.0005$; effect size, 89%; Fig. 5B) tDCS. Thresholds were similar when testing was repeated 30 min after tDCS ($P = 0.082$).

We examined the data of the anodal responders to determine whether any of the subjects showed the pattern predicted by our shift-gain hypothesis (decreased threshold during a-tDCS and increased threshold during c-tDCS). The majority (6/9) showed a decrease in discrimination threshold for both polarities of tDCS. Only one subject showed the predicted pattern. Interestingly, the nonresponders had the lowest baseline thresholds of all subjects in the anodal session, 3.8–5.5 μm. It is possible that a-tDCS could not induce a further decrease in threshold. In contrast, the baseline thresholds for the responders were higher, 6.5–13.5 μm (mean, 9 μm), but the percent decrease in threshold did not covary with threshold ($P > 0.8$ during and immediately after a-tDCS).

Finally, three subjects participated in both series of experiments (detection and discrimination), and they were categorized as anodal responders in both series (Figs. 4A and 5A). There were two differences: the magnitude of the effects in the discrimination task were relatively larger than in the detection task (note the change in scale) and especially pronounced after discrimination task was relatively larger than in the detection task. We also provide the first evidence showing that vibrotactile amplitude discrimination thresholds are reduced during and immediately after a-tDCS. Taken together, our results support our shift-gain hypothesis (Fig. 1) but only for a-tDCS.

As described in INTRODUCTION, we had expected that anodal stimulation would increase cortical excitability and reduce vibrotactile detection thresholds. Our results confirmed this prediction (mean decrease to 73% of baseline in the responders), and we interpret this as representing the result of a leftward shift of the stimulus-response curve. Thus weak stimuli that were subthreshold during the baseline testing became supraliminal in the presence of a-tDCS. This effect was short lasting, restricted to the testing carried out during and immediately after a-tDCS (see below). In a mostly separate group of subjects, we found that vibrotactile discrimination thresholds in the responders were also decreased during a-tDCS (to 76% of control) and immediately after tDCS (53%).

Finally, three subjects participated in both series of experiments (detection and discrimination), and they were categorized as anodal responders in both series (Figs. 4A and 5A). There were two differences: the magnitude of the effects in the discrimination task were relatively larger than in the detection task (note the change in scale) and especially pronounced after the end of a-tDCS.

**RT measures.** RT was measured in each trial, as this provided a second and independent measure of response certainty. As expected, median RT was significantly longer in the incorrect trials, 1,010 ms (25–75%; 692–1,298 ms) compared with correct trials, 869 ms (25–75%; 596–1,135 ms; $P < 0.0005$, Kruskal-Wallis), reflecting increased uncertainty. As also expected, RTs (correct) decreased significantly, as the amplitude of the comparison stimulus was increased ($P < 0.0005$).

The duration of each session was relatively long (2 h), and so fatigue was a potential confounding factor. To determine the contribution of fatigue to the results, we applied a regression analysis to the results from each subject (each session), RT (correct) vs. block number (1–5). If fatigue were a factor, then we expected that RT would systematically increase across the session. For the majority of the sessions (24/36), RT was stable across the five test blocks. A significant increase in RT was found for only three sessions (3 different subjects). In nine other sessions (8 subjects), there was a significant decrease in RT. The latter included the anodal session from three of nine responders. Overall, the results suggest that fatigue was not a major factor in this study.

**DISCUSSION**

The results confirm that S1 a-tDCS improves tactile perception. This is the first demonstration that weak a-tDCS of S1 leads to a reduction in vibrotactile detection threshold, during and immediately after the application of the stimulation. The reversal of the polarity of the stimulation did not, as expected, have the opposite effect; instead, there was no change in detection threshold. We also provide the first evidence showing that vibrotactile amplitude discrimination thresholds are reduced during and immediately after a-tDCS. Taken together, our results support our shift-gain hypothesis (Fig. 1) but only for a-tDCS.

Curiously, cathedral stimulation did not generate the opposite pattern of results. For both tactile tasks, detection and discrimination, no change was observed (vs. sham). This pattern of modulation (no effect with c-tDCS coupled with enhanced excitability with a-tDCS) has been reported by others (Jeffery et al. 2007; Matsunaga et al. 2004). There was, however, some suggestion of a decrease in discrimination threshold during c-tDCS (to 80% of baseline) in the anodal responders (Fig. 5B), but the results were not different from the sham testing. Whereas early reports (Liebetanz et al. 2002; Nitsche and Paulus 2000, 2001) stressed the polarity-dependent effects of tDCS on M1 cortical excitability, Wiethoff et al. (2014) recently reported, in a relatively large-scale study, that almost 50% of their subjects showed facilitation of M1 excitability with both polarities of tDCS stimulation to hand motor cortex, whereas the remainder showed no change. The latter findings are consistent with the present observations and undoubtedly reflect large intersubject differences in sensitivity to tDCS (see below).

We had expected that threshold would remain constant across the sham session. This was confirmed for the discrimination testing, but there was an unexpected increase in threshold across the s-tDCS testing for the detection task. This effect was restricted to the blocks during and after s-tDCS and was observed in both the anodal responders and nonresponders (Fig. 4B). The subjects had no knowledge of the nature of the stimulation applied (s-, a-, or c-tDCS), so this could not have influenced their performance. Since there was no such increase during the c-tDCS testing in anodal responders (detection task) and since the discrimination testing showed some evidence of increased thresholds during c-tDCS, again in anodal responders, it appears that c-tDCS did not have a modest effect on tactile perception, but the direction of the effect was the same as for a-tDCS, i.e., improved detection and discrimination. Moreover, there was some suggestion that these effects were part-
particularly seen in the anodal responders. These observations should be pursued in the future using higher intensities of stimulation than tested here, a relatively low intensity of 1 mA.

Our finding of a decrease in vibrotactile discrimination threshold during a-tDCS is in agreement with the results of Ragert et al. (2008), recently confirmed by Fujimoto et al. (2014). They found that tactile discrimination is improved during a-tDCS but in their case, with the use of a measure of spatial acuity (grating orientation test) that is considered to depend primarily on activation of slowly adapting type I mechanoreceptive afferents [Phillips and Johnson (1981); reviewed in Johnson (2001)]. Our tasks, in contrast, used low-frequency (20 Hz) vibration within the flutter range that is generally considered to be mediated by activation of rapidly adapting mechanosensitive afferents presumed to innervate Meissner corpuscles (Mountcastle et al. 1972). This observation suggests that the effects of a-tDCS are generalized, improving tactile discrimination dependent on different sources of afferent feedback. There was, however, one important difference. Ragert et al. (2008) reported that their effects outlasted the duration of stimulation, up to 40 min. Fujimoto et al. (2014) confirmed that the improvement in spatial acuity persists immediately after a-tDCS, but the effect was absent when testing was repeated 30 min later. Our results are consistent with those of Fujimoto et al. (2014) for both tasks: vibrotactile detection and discrimination.

The improvement in tactile perception with a-tDCS reported here and by others contrasts with the negative results (no effect) reported by Grundmann et al. (2011). Several factors may have contributed to their negative results, including a shorter duration for the tDCS (15 vs. 20 min here) and differences in both the test site (hand dorsum, a region with lower tactile sensitivity vs. the glabrous skin of the fingers) and the testing procedure (up and down staircases using manually applied von Frey filaments). More importantly, however, Grundmann et al. (2011) did not evaluate sensory perception during the application of the tDCS, and there is evidence that motor learning is enhanced with a-tDCS to M1 if the motor task is practiced during the stimulation [reviewed in Reis and Fritsch (2011)]. Evidence from animal research suggests that the beneficial effects of tDCS on motor learning may be linked to activity-dependent release of BDNF (Fritsch et al. 2010). Moreover, the latter study also showed that healthy individuals with a BDNF polymorphism show impaired motor-skill acquisition in a protocol with repeated daily sessions of a-tDCS combined with practicing a motor task. In a similar vein, Cheeran et al. (2008) reported that the aftereffects of plasticity-inducing protocols elicited by repetitive TMS are reduced in subjects with this same polymorphism. Thus active engagement in a perceptual task may be essential to generate positive results with a-tDCS.

In this study, there was some variability in the results across subjects, with 67% and 75% categorized as responders in the detection and discrimination tasks, respectively. Although we cannot discount the possibility that anatomical differences (location of S1) may have contributed to the variability, it may also, at least partly, be linked to intersubject differences in their sensitivity to a-tDCS. It is therefore noteworthy that the three subjects who participated in both tasks were categorized as anodal responders in both cases. This may have a genetic basis, since the proportion of nonresponders in this study (25–33%) is similar to the proportion of subjects with the BDNF polymorphism, val66met (28%), in a European-American population, as also studied here (Egan et al. 2003). For the discrimination task, however, the nonresponders had very low baseline thresholds, consistent with the lack of effect representing a ceiling effect, and so dependent on natural variations in tactile sensitivity. Whereas the nonresponders in the detection task did not have the lowest baseline thresholds, it is possible that they were nevertheless performing at their physiologically maximal level and that their threshold could not be reduced further. In this regard, it is interesting to note that mean detection threshold here (4.4 μm) was considerably lower than we had expected from Mountcastle et al. (1972). For 20 Hz vibration, we had expected threshold to be 10–15 μm; our lower threshold estimates were, in fact, close to those reported more recently by Brisben et al. (1999).

In conclusion, we demonstrated that weak, 1 mA a-tDCS, applied to S1, produces an improvement in vibrotactile detection and discrimination in the majority of subjects. The underlying neuronal mechanisms were identified: a shift of the stimulus-response function to the left (decreased detection threshold) and an increase in its gain (decreased discrimination threshold). Future experiments should examine whether higher-intensity a-tDCS might produce greater and/or more consistent improvements in tactile perception and whether these effects might, as shown for motor-skill acquisition, be cumulative over time. Indeed, there is recent evidence that tactile sensory deficits in patients with multiple sclerosis are diminished with repeated S1 a-tDCS sessions (Mori et al. 2013). This leads to the interesting possibility that a-tDCS to S1 cortex might be a useful adjunct for the rehabilitation of stroke patients with sensory deficits affecting the hand region (Dannenbaum and Dykes 1988). It is known that sensory feedback relayed from S1 to M1 is critically important for hand motor control (Brochier et al. 1999; Hikosaka et al. 1985) and that hand motor control is particularly difficult to re-establish poststroke. Finally, our shift-gain hypothesis, supported only for a-tDCS, leads us to predict that measures of the subjective intensity of tactile stimuli should be increased during S1 a-tDCS and that the slope of the psychophysical function, relating subjective intensity to the amplitude of the stimulus, should be increased. This prediction will be tested in future experiments.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.
AUTHOR CONTRIBUTIONS

Author contributions: S.L. and C.E.C. conception and design of research; S.L., E.-M.M., and C.E.C. performed experiments; S.L. and C.E.C. analyzed data; S.L., E.-M.M., and C.E.C. interpreted results of experiments; S.L. and C.E.C. edited and revised manuscript; S.L., E.-M.M., and C.E.C. approved final version of manuscript.

REFERENCES


