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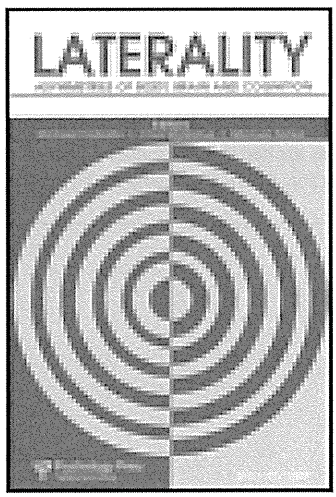
*Supplementary material to article by Y. Kasashima-Shindo et al. "Brain–computer interface training combined with transcranial direct current stimulation in patients with chronic severe hemiparesis: proof of concept study"*

APPENDIX SI. Assessment of mu event-related desynchronization (ERD)

Electroencephalography (EEG) signals were recorded with 22 Ag–AgCl disc electrodes with binaural references according to the International 10–20 system of electrode placement with the average of bilateral earlobe references. Impedance for all channels was maintained below 10 kΩ throughout the experiment. Electromyograms were simultaneously recorded from the bilateral EDC with surface Ag–AgCl disc electrodes to monitor electromyographic (EMG) activities during the imagery task to avoid unexpected muscle contraction. EEG and EMG signals were amplified, digitized with a sampling frequency of 1000 Hz and bandpass filtered (EEG 0.53–100 Hz, EMG 20–1 kHz) using a commercially available bio-signal recorder (Neurofax EEG-9100, Nihon Kohden Corporation, Japan).

The participants sat in an upright position in an armchair. Their eyes were open, and they were facing the computer monitor that displayed the task. The monitor was placed approximately 50 cm in front of the subject at eye level. One trial started with a 10-s period of relaxation during which the word "Rest" was shown on the monitor. After that, the word "Image" was presented for 5 s, and the participants were asked to imagine extension of their affected fingers. The trial ended when the word "Rest" reappeared. After that, the next trial began. To avoid a learning effect, they were given no feedback regarding EEG changes. One session consisted of 20 trials, and the 2 sessions were performed with approximately 5-min rest periods between each session.

The values of mu ERD on the affected motor area (C3 and FC3, or C4 and FC4) were calculated. The same electrodes used in the BCI training were chosen. Event-related trials lasting 5 s during motor imagery were selected for off-line data processing. All trials were visually assessed. The trials with artefacts resulting from eye movement and the trials with increased EMG activity were excluded. All trials were segmented into successive 1-s windows with 900 overlapping samples, and the Fourier transform with the Hanning window was applied to each segment. The power spectral density of each segment was estimated over the trials using Welch's averaged periodogram method (36). All off-line analysis of EEG data was performed using MATLAB (The MathWorks, Inc., USA).



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# Transcranial direct current stimulation enhances mu rhythm desynchronization during motor imagery that depends on handedness

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# Transcranial direct current stimulation enhances mu rhythm desynchronization during motor imagery that depends on handedness

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Transcranial direct current stimulation (tDCS) can modulate the amplitude of event-related desynchronization (ERD) that appears on the electroencephalogram (EEG) during motor imagery. To study the effect of handedness on the modulating effect of tDCS, we compared the difference in tDCS-boosted ERD during dominant and non-dominant hand motor imagery. EEGs were recorded over the left sensorimotor cortex of seven healthy right-handed volunteers, and we measured ERD induced either by dominant or non-dominant hand motor imagery. Ten minutes of anodal tDCS was then used to increase the cortical excitability of the contralateral primary motor cortex (M1), and ERD was measured again. With anodal tDCS, we observed only a small increase in ERD during non-dominant hand motor imagery, whereas the same stimulation induced a prominent increase in ERD during dominant hand motor imagery. This trend was most obvious in the participants who used their dominant hand more frequently. Although our study is preliminary because of a small sample size, these results suggest that the increase in ERD by applying anodal tDCS was stronger on the dominant side than on the non-dominant side. The background excitability of M1 may determine the strength of the effect of anodal tDCS on ERD by hand motor imagery.

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***Keywords:*** Transcranial direct current stimulation; Electroencephalogram; Event-related desynchronization; Handedness; Motor cortex.



The mu rhythm is a spontaneous characteristic feature of the electroencephalogram (EEG)/magnetoencephalogram pattern. It consists of 8–13 Hz activities that appear maximally over the central rolandic or sensorimotor areas during a relaxed state (Pfurtscheller, Neuper, Andrew, & Edlinger, 1997; Pfurtscheller, Stancak, & Neuper, 1996). The mu rhythm is attenuated by tactile stimulation, movement execution and motor imagery, a process referred to as event-related desynchronization (ERD; Arroyo et al., 1993; Kozelka & Pedley, 1990; Kuhlman, 1978). Such ERD of the mu rhythm, named mu ERD in this study, is interpreted as the desynchronized activities of the activated neurons based on externally or internally paced events (Pfurtscheller & Lopes da Silva, 1999).

Recent studies infer that mu ERD when preparing for contralateral extremity movement is somehow related to cortical activity. For instance, increased excitability of the contralateral corticospinal tract (Facchini, Muellbacher, Battaglia, Boroojerdi, & Hallett, 2002; Kasai, Kawai, Kawanishi, & Yahagi, 1997) has been observed during motor imagery of hand muscles, which is a task known to induce mu ERD. Also during motor imagery and movement, the contralateral decrease of alpha/beta EEG (i.e., mu ERD was presumably present) co-localized with an increase of the blood-oxygen-level dependent signal in the primary sensorimotor cortex in functional magnetic resonance imaging (Yuan et al., 2010). More recently, association of mu ERD of contralateral corticospinal tract excitability and GABAergic interneuronal disinhibition in the primary motor cortex (M1) was reported (Takemi, Masakado, Liu, & Ushiba, 2013). Based on these findings, neurofeedback or Brain–Computer Interface (BCI), an EEG operant-conditioning training technique with mu ERD, may offer a new strategy to train the voluntary regulation of corticospinal excitability for functional recovery in people with severe motor disabilities following stroke (Ang et al., 2011; Birbaumer & Cohen, 2007; Broetz et al., 2010; Buch et al., 2008; Caria et al., 2011; Daly & Wolpaw, 2008; Mukaino et al., 2014; Prasad, Herman, Coyle, McDonough, & Crosbie, 2009; Ramos-Murguialday et al., 2013; Shindo et al., 2011). More recently, combining mu ERD-based BCI rehabilitation with active physical therapy or with functional electrical stimulation may improve the motor abilities of chronic stroke patients (Broetz et al., 2010), revealing the potential therapeutic utility of mu ERD-based BCI rehabilitation.

Transcranial direct current stimulation (tDCS), which involves applying a weak direct current through the scalp, is another candidate for increasing cortical excitability. Anodal tDCS is known to induce long-lasting facilitatory effects (Nitsche & Paulus, 2001), confirmed by changes in the motor evoked potential (MEP; Nitsche & Paulus, 2000, 2001), blood oxygenation level (Baudewig, Nitsche, Paulus, & Frahm, 2001) and regional cerebral blood flow

(Kwon et al., 2008; Lang et al., 2005; Merzagora et al., 2010). These effects of tDCS may have the potential to facilitate the efficacy of mu ERD-based BCI rehabilitation. Matsumoto et al. (2010) actually found that mu ERD by hand motor imagery increased significantly after anodal stimulation. However, the effect of hand dominance on ERD remains unknown. The mechanisms of motor control and learning are different between the dominant and non-dominant hand (Duff & Sainburg, 2007; Schabowsky, Hidler, & Lum, 2007; Yokoi, Hirashima, & Nozaki, 2014). For example, Duff and Sainburg (2007) found that interlimb differences in motor control produce different patterns of adaptation to novel dynamics. Recently, Yokoi et al. (2014) showed interlimb differences in how adaptation to novel dynamics in one arm is influenced by the kinematics of the opposite arm. Thus, the effect of anodal tDCS on the improvement of mu ERD by hand motor imagery might be different between the dominant and the non-dominant hand.

To assess this issue, we asked participants to perform either dominant or non-dominant hand motor imagery before and after anodal tDCS to the corresponding hemisphere and investigated its effect on changes in mu ERD.

## METHODS

### Participants

This study involved seven right-handed healthy participants (6 males, 1 female; mean age, 25 ± 4 years; age range, 22–31 years). Participants were informed about all aspects of the experiments and all gave informed consent. No participant had a history of neurological disease or was receiving any acute or chronic medication affecting the central nervous system. Handedness was tested using the Edinburgh Handedness Inventory (Oldfield, 1971). Laterality Quotient (LQ), which ranges from −1.0 to +1.0 (+, right-handed; −, left-handed; near 0, ambidextrous), was obtained from each participant. All participants were judged as right-handed, with an LQ range of 0.5–1.0. This study was carried out in accordance with the Declaration of Helsinki and was approved by the local ethics committee.

### Data recording

EEG signals were recorded from 15 Ag/AgCl disc electrodes (1 cm in diameter) according to the international 10–20 system of electrode placement (FC3, FC1, FCz, FC2, FC4, C3, C1, Cz, C2, C4, CP3, CP1, CPz, CP2, CP4) with the average of left and right earlobe references to cover the motor areas of both hands and occipital area. Using the belly-tendon method, an electromyogram (EMG) was simultaneously recorded from the left and right first dorsal interosseous (FDI) muscles with surface Ag/AgCl disc electrodes (1 cm in

diameter) to confirm EMG activity during imagery tasks and to avoid unexpected muscle contraction. EEGs and EMGs were amplified and digitized (1000 Hz sampling frequency) using a commercially available biosignal recorder (Neurofax EEG-9100, Nihon Kohden Corporation, Japan). Impedance was kept below 10 kΩ during the whole experiment.

## Experimental paradigm

The experimental design of the present study was previously established elsewhere (Matsumoto et al., 2010) and also described below.

Experiments took place on four different days, each separated from the preceding one by more than one week for the same participant. On each experimental day, the following paradigm was examined with either left- or right-hand motor imagery, and either anodal or sham stimulation prior to the task. The hand for motor imagery and type of stimulation were randomly chosen for each individual.

Participants sat in an armchair with their eyes open facing a computer monitor placed approximately 0.9 m in front of them at eye level. A trial started with an 8-s resting-state period during which the word "Rest" was shown at the centre of the monitor. After that was a 2-s period during which the word "Ready" was shown. Then, the word "Start" was presented for 5 s, and participants were asked to imagine their hand grasping. The trial ended when the word "Rest" reappeared, and the next trial began after a break of 8 s (Figure 1a). Participants were given no feedback about EEG changes to avoid a learning effect. One session consisted of 20 trials, and four sessions were conducted before and after

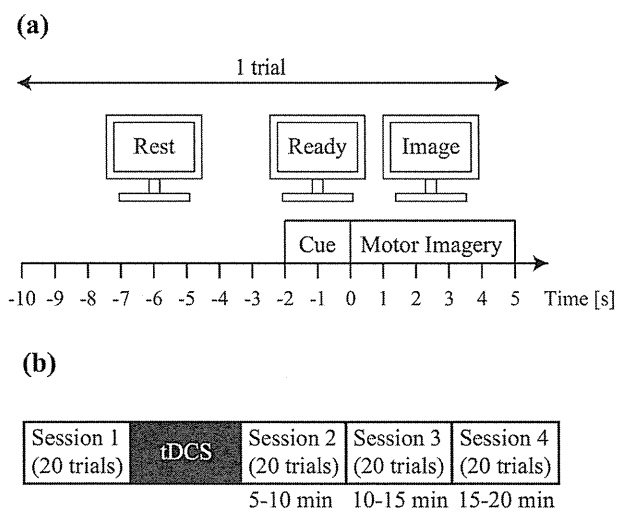


**Figure 1.** The experimental paradigm used in this study (Redrawn from Matsumoto et al., 2010).

tDCS (Figure 1b). There were breaks for about 5 min between sessions. All four sessions were completed within 30 min.

## Transcranial direct current stimulation

Bipolar stimulation was delivered by a battery-driven stimulator (CX-6650, Rolf Schneider Electronics, Gleichen, Germany) through a pair of rectangular water-soaked sponge electrodes ($50 \times 70$ mm$^2$). The current intensity was set at 1 mA and the ramp time was set at 5 s, and the stimulation was administered for 10 min. The position of M1 was confirmed through the induction of the largest MEPs in the right FDI muscle with constant stimulus intensity using transcranial magnetic stimulation (TMS) with a figure-eight stimulation coil connected to a Magstim 200 magnetic stimulator (Magstim, Whitland, UK). One electrode was placed over the M1 contralateral to the hand of imagery, and the other was placed over the right supraorbital area.

The stimulation protocol described below was previously established (Matsumoto et al., 2010; Nitsche et al., 2008) and also used in this study. For the sham stimulation, the current was applied for only 10 s to mimic the transient skin sensation at the beginning of actual tDCS without producing any conditioning effects on the brain. Participants were blinded to stimulation condition. For placing the stimulation electrode, three to four EEG electrodes over the stimulus site were removed after marking the scalp. After the tDCS stimulation, the EEG electrodes were set in the same position as before. Impedance was confirmed to be 10 k$\Omega$, similar to the situation prior to tDCS. It took less than 3 min for electrode replacement, and thus the effect of elapsed time after tDCS on ERD measurement was limited.

## Quantification of ERD and statistical analysis

Event-related trials 5 s in duration during motor imagery were selected for offline data processing. All trials were visually assessed, and trials with artefacts (resulting from eye movement) as well as trials with increased EMG activity of the right FDI were excluded. All trials were segmented into successive 1-s windows with 900 overlapping samples, and the Fourier spectrum density in each segment was calculated with a Hamming window. The mu ERD was expressed as the percentage power decrease in relation to a 2-s reference interval before the "Ready" instruction. The ERD was calculated for each time point (resolution of 0.1 s) and frequency according to Equation (1):

$$\mathrm{ERD}(f,t) = \frac{R(f) - A(f,t)}{R(f)} \times 100(\%) \tag{1}$$

where $A$ is the power spectrum density of the EEG at a certain frequency $f$ [Hz], time $t$ [s] is the duration from the start of the imagery task and $R$ is the power spectrum at the same frequency $f$ [Hz] of the baseline period (a 1-s interval before the "Ready" instruction was displayed). A large positive value indicates a large power decrease during motor imagery compared with that at rest. ERD was calculated in each trial and then averaged over 60 times for pre- and post-tDCS sessions. Only in cases where the ERD time course was assessed after tDCS, ERD was calculated with 20 averages each, and a total of 3 epochs (5–10 min, 10–15 min and 15–20 min after tDCS) were obtained (Figure 1b). The strongest power decrease during motor imagery was selected as the value of mu ERD. Before tDCS application, the values of mu ERD were compared in all adjacent pairs of bipolar derivations of EEG, and then we determined the electrode pair showing the strongest value of mu ERD for each individual. Then, the values of mu ERD in two stimulation conditions (anodal and sham stimulation) were calculated from the same bipolar derivation of EEG. All offline analyses of EEG data were performed using MATLAB (The Mathworks Inc., USA).

A two-way repeated measures analysis of variance (ANOVA; time × hand) was used to compare (1) the mu ERD during imagery with main factors of time (before and 5–10 min, 10–15 min and 15–20 min after tDCS) and side of motor imagery (right and left) and (2) the mu ERD during imagery with main factors of time (before and after sham stimulation) and side of motor imagery (right and left). We could not directly compare (1) with (2) because the number of time points was different between conditions. Therefore, we performed a three-way repeated measures ANOVA (time × hand × condition) using the data before anodal tDCS and data from the average of three time periods after the anodal tDCS, and the data before and after sham stimulation. If statistical analysis yielded a significant $F$ value ($P < 0.05$), a post hoc Bonferroni test was carried out.

## RESULTS

None of the participants reported any adverse effects of tDCS during or after the experiments. All participants showed mu ERD over the sensorimotor cortex contralateral to the hand of motor imagery during motor imagery before tDCS. The electrode pairs that showed the strongest mu ERD varied between individuals. Further analysis was performed with the electrode pairs that in each participant showed the strongest mu ERD to assess the effect of anodal stimulation on mu ERD by motor imagery.

Typical examples of the effect of anodal tDCS on EEG power spectrum densities are shown in Figure 2a and b. Averaged EEG power spectrum densities are shown in Figure 2c and d. Mu EEG power increased in both rest and motor imagery periods. The increase was significant in the left hemisphere

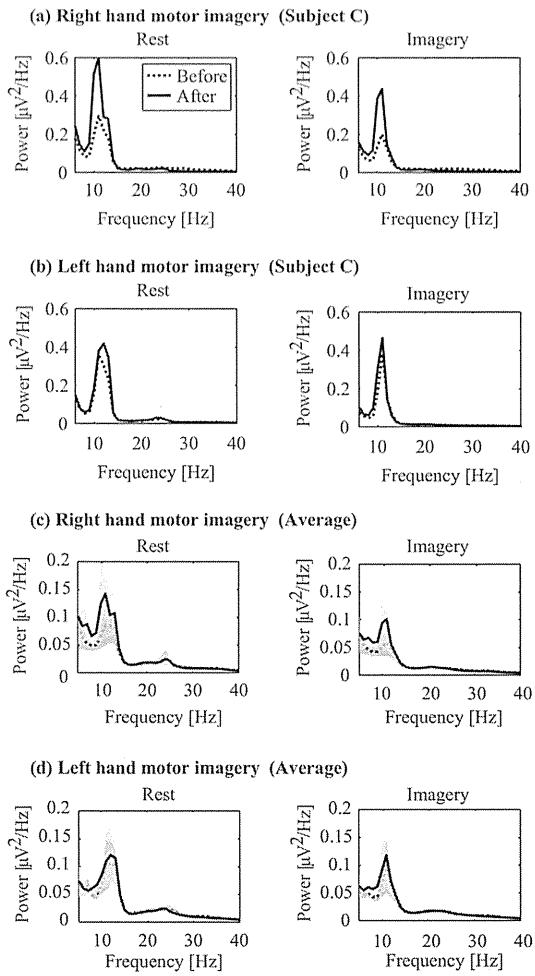


**Figure 2.** EEG power spectrum densities before and after tDCS during rest or motor imagery periods. (a) Typical examples of EEG power spectrum densities during rest or right-hand motor imagery periods (participant C). The mu EEG power component was increased after tDCS in both rest and motor imagery periods. Dotted lines indicate data before stimulation and solid lines indicate data after stimulation. (b) Typical examples of EEG power spectrum densities during rest or left-hand motor imagery periods (participant C). The mu EEG power component was increased after tDCS in rest periods but was almost unchanged in motor imagery periods. Dotted lines indicate data before stimulation and solid lines indicate data after stimulation. (c) Averaged EEG power spectrum densities during rest or right-hand motor imagery periods across all participants. Dotted lines indicate data before stimulation and solid lines indicate data after stimulation. Shaded areas indicate standard error. (d) Averaged EEG power spectrum densities during rest or left-hand motor imagery periods across all participants. Dotted lines indicate data before stimulation and solid lines indicate data after stimulation. Shaded areas indicate standard error.

during right-hand (dominant) motor imagery (Figure 3). The mean (standard deviation, s.d.) increase of mu EEG was 230.6% (293.2%) in the rest period and 177.1% (196.4%) in the motor imagery period. During left-hand (non-dominant) motor imagery, mu ERD power also increased in both rest and imagery periods in some participants, but their increase in amplitudes were limited. For this reason, the mean (s.d.) of the change of mu EEG among the participants remained almost unchanged: 108% (30.3%) in the rest period and 115.9% (47.1%) in the motor imagery period.

Mu ERD is calculated from the EEG power of the alpha band in the motor imagery period divided by the power during the rest period. To compare the change in Mu ERD before and after stimulation between hands (i.e., right and left) and conditions (i.e., sham and anodal; Figure 4), we performed a three-way repeated measures ANOVA. There was a significant effect of time, $F(1, 48) = 4.98$, $p < 0.05$, and condition, $F(1, 48) = 4.09$, $p < 0.05$. The effect of hand was not significant, $F(1, 48) = 0.39$, $p = 0.53$ (Table 1). A post hoc test indicated that there was a significant difference between conditions in the dominant hand after stimulation ($p < 0.01$; Bonferroni corrected), and a significant difference between before and after tDCS in the anodal stimulation condition in the dominant hand ($p < 0.05$; Bonferroni corrected; Figure 4a). The difference in condition for mu ERD before stimulation was not significant (dominant hand, $p = 0.84$; non-dominant hand, $p = 0.65$; Bonferroni corrected).

Enhancement of mu ERD by anodal tDCS during right-hand (dominant) motor imagery in which the data from three time periods after the tDCS were averaged is shown in Figure 5. Mu ERD following motor imagery was enhanced in all participants. The mean (s.d.) mu ERD value before anodal stimulation was 41.6% (27.5%) and was 58.4% (23.2%) after anodal stimulation. A paired $t$-test confirmed a significant difference, $t(7) = 3.3$, $p < 0.05$. In the case of left-hand (non-dominant) motor imagery, tDCS also enhanced mu ERD following motor imagery, but the effect was smaller than during dominant hand motor imagery as only 4 of 7 participants showed an increase in ERD. The mean (s.d.) mu ERD value before anodal stimulation was 46.8% (28.3%) and was 49.4% (24.4%) after anodal stimulation; this change was not statistically significant, $t(7) = 0.32$, $p = 0.76$.

When we investigated temporal changes in mu ERD after the stimulation, mu ERD was strongest during right-hand (dominant) motor imagery not immediately, but 15–20 min after anodal stimulation (Figure 5a), and it slowly decayed. A two-way repeated measures ANOVA detected a significant main effect of time, $F(3, 45) = 3.1$, $p < 0.05$, and an interaction effect, $F(3, 45) = 4.8$, $p < 0.01$. There was no effect of hand, $F(1, 45) = 1.9$, $p = 0.18$ (Table 1). A post hoc test showed that there was a significant increase in mu ERD between before and 15–20 min after the stimulation ($p < 0.01$, Bonferroni corrected). Conversely, during left-hand (non-dominant) motor imagery, the time course of mu ERD after tDCS

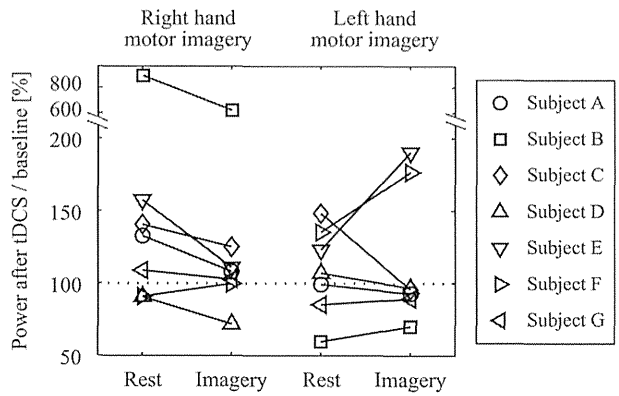


**Figure 3.** Pooled data of increase in mu EEG by anodal tDCS. A similar increase to that shown in a single case (Figure 2a and b) was also seen.

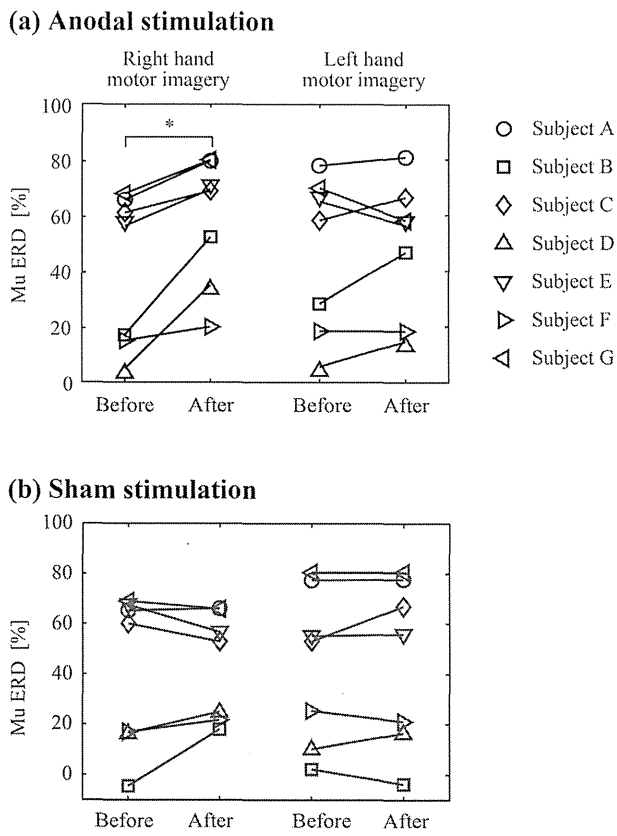


**Figure 4.** Mu ERD before and after anodal/sham tDCS during right- and left-hand motor imagery. (a) Mu ERD before and after anodal stimulation. (b) Mu ERD before and after sham stimulation. $*p < 0.05$.

TABLE 1
ANOVA

| *Source of variance* | *Sum of squares* | *Degrees of freedom* | *Mean squares* | F | P |
|---|---|---|---|---|---|
| A three-way repeated measures ANOVA for two conditions | | | | | |
| Time | 408.6327 | 1 | 408.6327 | 4.9799 | 0.0310 |
| Hand | 32.3053 | 1 | 32.3053 | 0.3937 | 0.5338 |
| Condition | 335.3060 | 1 | 335.3060 | 4.0863 | 0.0496 |
| Time × hand | 61.3339 | 1 | 61.3339 | 0.7475 | 0.3922 |
| Hand × condition | 165.4012 | 1 | 165.4012 | 2.0157 | 0.1631 |
| Time × condition | 258.7495 | 1 | 258.7495 | 3.1533 | 0.0830 |
| Time × hand × condition | 506.6890 | 1 | 354.1075 | 4.3154 | 0.0439 |
| Error | 3446.3959 | 48 | 82.0570 | | |
| Total | 5214.8135 | 55 | | | |
| A two-way repeated measures ANOVA for anodal stimulation condition when sessions after the stimulation were separately analyzed | | | | | |
| Time | 1077.0017 | 3 | 359.0006 | 3.1311 | 0.0364 |
| Hand | 214.1468 | 1 | 214.1468 | 1.8677 | 0.1796 |
| Time × hand | 1644.4477 | 3 | 548.1492 | 4.7808 | 0.0062 |
| Error | 4471.6119 | 45 | 114.6567 | | |
| Total | 7407.2082 | 52 | | | |



varied among the participants, and no common pattern was observed (Figure 5b). The time at which mu ERD peaked was different in each participant.

As mentioned above, anodal tDCS promoted a large mu ERD during right-hand (dominant) motor imagery, but a small mu ERD was observed during left-hand (non-dominant) motor imagery. To account for this, we hypothesized that participants who almost always use their dominant hand in daily life may show this trend the strongest. Therefore, we examined the relationship between degree of handedness (rated using LQ in the Edinburgh Handedness Inventory) and the laterality of ERD (ERD during right-hand (dominant) motor imagery after tDCS *minus* ERD during left-hand (non-dominant) motor imagery after tDCS). Figure 6 shows a positive correlation between LQ and the laterality of tDCS-boosted ERD, $r = 0.72$, $p < 0.05$.

## DISCUSSION

Cortical activation can result in phasic changes in the synchrony of cell populations because of externally or internally paced events and produce characteristic EEG patterns. Mu ERD is thought to arise from a decrease in the synchrony of the underlying neuronal population at the frequency of interest (Pfurtscheller & Lopes da Silva, 1999). Consistent with our previous study (Matsumoto et al., 2010), the present study shows that anodal tDCS on M1 increased mu ERD. This might be because of the increase of cortical excitability by anodal stimulation, such as

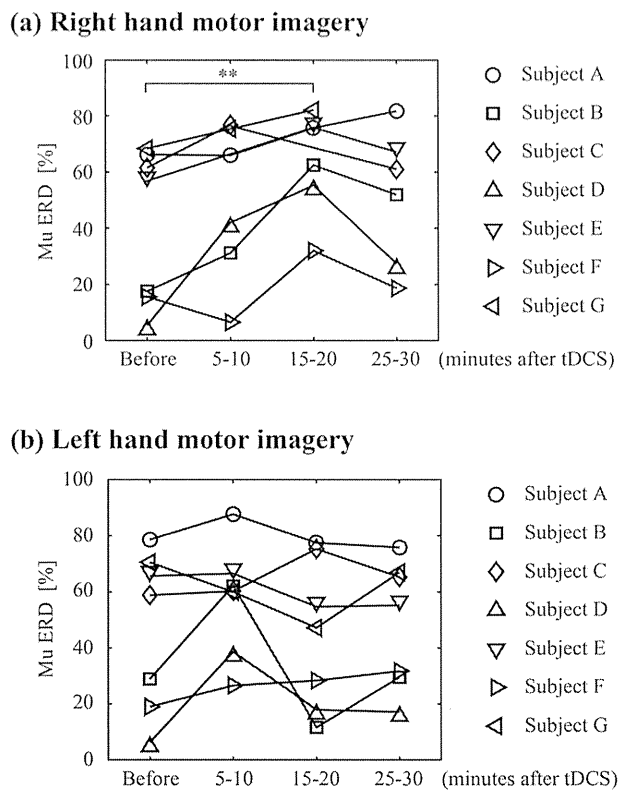


**Figure 5.** Time course of mu ERD after anodal tDCS. (a) Time course of mu ERD after anodal simulation during right-hand motor imagery. Mu ERD was significantly stronger around 15–20 min after tDCS compared with that before stimulation.**$p < 0.01$. (b) Time course of mu ERD after anodal simulation during left-hand motor imagery. Mu ERD was enhanced immediately after stimulation and rapidly decayed.

modifications of membrane depolarization (Bindman, Lippold, & Redfearn, 1964; Nitsche, Fricke, et al., 2003; Nitsche & Paulus, 2000, 2001; Purpura & McMurtry, 1965; Terzuolo & Bullock, 1956), increases in spontaneous firing rate (Bindman et al., 1964; Purpura & McMurtry, 1965) and other synaptic mechanisms (Nitsche, Nitsche, et al., 2003, Nitsche et al., 2005). These mechanisms may cause changes in the oscillatory activity of cortical neurons according to input signals in response to motor imagery and thus increase mu ERD.

The present study first showed that anodal tDCS promoted a large mu ERD during right-hand (dominant) motor imagery, but not during left-hand (non-dominant) motor imagery. This difference between the dominant and the non-dominant hand in motor control and learning reported in previous studies (Duff & Sainburg, 2007; Schabowsky et al., 2007) is similar to that during motor imagery. Moreover, this trend of the effect of tDCS was more prominent in participants who use their right hand the most in daily life.

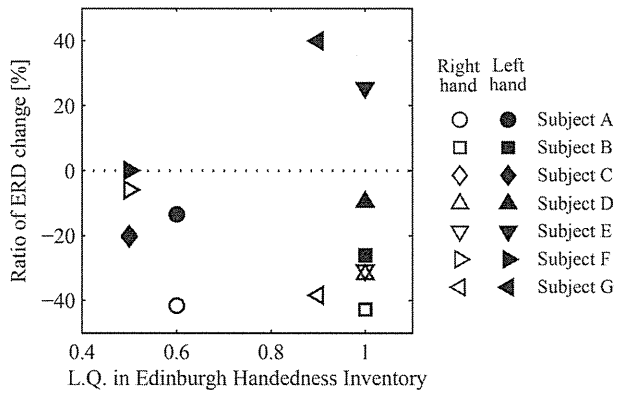


**Figure 6.** Ratio of change of mu ERD during right- and left-hand motor imagery. Ratio of ERD changes in participants who had low LQ scores was almost the same between right- and left-hand motor imagery. However, ERD ratio changes were different in participants who had high LQ scores.

These findings support our hypothesis that these diminished effects of tDCS on the non-dominant hand are due to lower cortical activity during non-dominant hand motor imagery. Voluntary movement is preceded by increased activity of corticospinal neurons in animal recordings (Evarts, 1966). A comparison between mu ERD and corticospinal excitability measured by TMS in reaction time paradigms demonstrates that mu ERD may be associated with contralateral corticospinal facilitation and ipsilateral corticospinal inhibition (Leocani, Toro, Zhuang, Gerloff, & Hallett, 2001). Thus, the varying degree of mu ERD change could conceivably reflect differences in the density, excitability or synaptic efficacy of these corticospinal efferents. In right-handed people, the threshold for activation of muscles in the right arm was lower than that of corresponding muscles in the left arm (Triggs, Calvanio, Macdonell, Cros, & Chiappa, 1994), and in particular, consistency of hand preference is associated with lateralized differences in the excitability of motor system projections activated by TMS (Macdonell et al., 1991; Triggs et al., 1994). Moreover, the upstream brain regions of the primary sensorimotor cortex, associated with motor planning, also shows hemispheric asymmetry (Sabaté, González, & Rodríguez, 2004). Therefore, the difference in the tDCS effect might be associated with asymmetries of excitability in the corticospinal tract. A smaller increase in the excitability of the corticospinal tract descending to the left-hand (non-dominant) muscle might be induced by tDCS during left-hand (non-dominant) imagery, because motor imagery may fail to activate a large number of neurons with high motor thresholds. However, because we did not check cortical excitability in this experiment, using TMS for example, we cannot strongly conclude this. Considering evidence that there are hemispheric differences in sensitivity to tDCS (Schade, Moliadze, Paulus, & Antal, 2012), it is also possible that the hand

difference we found was caused by differences in sensitivity to tDCS. Further control experiments of left-handed participants, for instance, are necessary.

The effect of anodal tDCS during right-hand motor imagery increased the most at 15–20 min after stimulation and began to gradually decay, but continued for more than 30 min. The after-effect of tDCS on cortical excitability resembles a long-term potentiation (LTP)-like or long-term depression (LTD)-like mechanism. Several studies using tDCS or other transcranial stimulation methods to induce excitability changes reported a delayed peak in the effect (minutes after the end of stimulation; Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005; Kuo, Grosch, Fregni, Paulus, & Nitsche, 2007; Kuo et al., 2008; Merzagora et al., 2010; Nitsche et al., 2006). Delayed LTP and LTD are also common findings in animal studies (Fernández de Sevilla, Núñez, Borde, Malinow, & Buño, 2008; Raymond, 2007). The similar delay we found probably reflects a physiological LTP-like cortical response to tDCS. The prolonged effect was not seen on mu ERD during left-hand (non-dominant) motor imagery. This may be also because of the lesser effect of tDCS on the non-dominant side.

Care should be taken in interpreting the current results because of the relatively small sample size. However, as a preliminary study, the present data show that cortical excitability is closely related to the ratio of activated and desynchronized neurons during motor imagery, and that: (1) anodal tDCS increased cortical excitability and thus promoted the enhancement of mu ERD; (2) the enhancement of mu ERD following non-dominant hand motor imagery by tDCS was also observed, although it was less than that following dominant hand motor imagery; (3) participants who used their dominant hand daily showed a stronger asymmetric effect of tDCS and a weaker effect on mu ERD during non-dominant hand motor imagery; and (4) the effect of tDCS on mu ERD during dominant hand motor imagery increased the most at 15–20 min after the stimulation and gradually decayed afterward but persisted for more than 30 min. However, the effect of tDCS on mu ERD during non-dominant hand motor imagery increased immediately and decayed rapidly. These results suggest that the background excitability of M1 may determine the strength of the effect of anodal tDCS on ERD by hand motor imagery and the greater excitability of M1 promotes larger effects of tDCS on ERD. Considering the possibility that BCI neurofeedback training with active physical therapy or with functional electric stimulation may improve the motor abilities of chronic stroke patients (Broetz et al., 2010), it might also be effective to combine tDCS with BCI training to improve BCI training's effectiveness.

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