Differential effects of primary motor cortex and cerebellar transcranial direct current stimulation on motor learning in healthy individuals: A randomized double-blind sham-controlled study

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A B S T R A C T

The purpose of study was to compare the effect of primary motor cortex (M1) and cerebellar anodal transcranial direct current stimulation (a-tDCS) on online and offline motor learning in healthy individuals. Fifty-nine healthy volunteers were randomly divided into three groups (n = 20 in two experimental groups and n = 19 in sham-control group). One experimental group received M1a-tDCS and another received cerebellar a-tDCS. The main outcome measure were response time (RT) and number of errors during serial response time test (SRTT) which were assessed prior, 35 min and 48 h after the interventions. Reduction of response time (RT) and error numbers at last block of the test compared to the first block was considered online learning. Comparison of assessments during retention tests was considered as short-term and long-term offline learning. Online RT reduction was not different among groups (P > 0.05), while online error reduction was significantly greater in cerebellar a-tDCS than sham-control group (P < 0.017). Moreover, a-tDCS on both M1 and cerebellar regions produced more long-term offline learning as compared to sham tDCS (P < 0.01), while short-term offline RT reduction was significantly greater in M1a-tDCS than sham-control group (P < 0.05). The findings indicated that although cerebellar a-tDCS enhances online learning and M1a-tDCS has more effect on short-term offline learning, both M1 and cerebellar a-tDCS can be used as a boosting technique for improvement of offline motor learning in healthy individuals.

1. Introduction

Motor skills play an important role during individuals life (Stodden et al., 2008). People need to learn or relearn motor skills during their daily activities or during therapeutic interventions following neurological disorders (Shumway-Cook and Woollacott, 1995; Krakauer, 2006). Thus, the learning during or following motor training for skill acquisition is an important part of healthy living and implementation of therapeutic approaches in patients with movement disorders (Shumway-Cook and Woollacott, 1995; Hall et al., 2011). In the past two decades, transcranial direct current stimulation (tDCS) was considered as an important neuromodulatory technique in clinical neuroscience (Reis et al., 2008; Nitsche and Paulus, 2000; Nitsche and Paulus, 2001). tDCS is a non-invasive technique which has been used to modulate cortical excitability and to facilitate skill acquisition during motor learning (Boggio et al., 2006; Hunter et al., 2009; Nitsche et al., 2003; Rosenkranz et al., 2000; Hummel and Cohen, 2006). tDCS effects are polarity dependent. Application of positive electrode over the brain’s target area (anodal tDCS, a-tDCS) increases cortical excitability but application of negative electrode (cathodal tDCS, c-tDCS) induces opposite effects (Nitsche and Paulus, 2000). Literature indicates that different cortical regions such as the primary motor cortex (M1), premotor and supplementary motor cortex, cerebellum, and basal ganglia are part of a network, which contribute to acquisition of motor skills during motor learning (Ungerleider et al., 2002; Doya, 2000; Krings et al., 2000). In this line of research, some studies reported that a-tDCS of M1 enhances motor performance and motor learning (Boggio et al., 2006; Nitsche et al., 2003; Hummel and Cohen, 2006; Vines et al., 2008; Hummel et al., 2005; Antal et al., 2004; Reis et al., 2009). Some other studies also indicated improvement in motor learning following cerebellar a-tDCS (Ferrucci et al., 2013; Galea et al., 2009; Hardwick and Celnik, 2014). It was...
evidenced that the cerebellum, as a learning machine (Albus, 1971; Marr and Thach, 1991), contributes in procedural motor learning and plays a major role in structuring motor skills, perceptions, and motor behavior (Hardwick and Celnik, 2014; Meltzoff et al., 2009; Dayan and Cohen, 2011; Gilbert and Thach, 1977; Kitazawa et al., 1998). It seems that cerebellum plays a crucial role in reducing errors related to new environmental demands during motor learning processing (Kitazawa et al., 1998; Tseng et al., 2007), while, M1 contributes to motor adaptation of skills by maintaining error corrections during motor learning (Galea et al., 2011). In this regard, Galea et al. (2011) compared online and short-term offline effects of a-tDCS of cerebellum and M1 on motor learning during a visuomotor task. They found that cerebellar a-tDCS caused faster adaptation to the visuomotor task, while M1 a-tDCS enhanced retention of the newly learnt visuomotor task (Galea et al., 2011). In contrast, Herzfeld et al. (2014) compared online and offline effects of cerebellar and M1 a-tDCS on motor learning during a motor force field task and also assessed lasting of the effects up to 24 h after the completion of the stimulation. Herzfeld et al. (2014) indicated that retention of task was not improved by M1 anodal stimulation (Herzfeld et al., 2014). However, there was controversy in the results of these studies (Galea et al., 2011; Herzfeld et al., 2014).

To the best of our knowledge, there is no study in the literature to collectively declare the effects of M1 or cerebellar a-tDCS on the size and lasting of the induced enhancement of motor performance.

The findings in this study will help to determine more effective a-tDCS interventions for induction of both online and offline effects on motor learning. Therefore, the purpose of the present study was to compare the effect of M1 and cerebellar a-tDCS on the response time (RT) and number of errors during and after completion of a motor training task. We hypothesized that, compared to M1 a-tDCS, stimulation of cerebellum induces more profound effects on online and offline motor learning.

2. Method and materials

2.1. Participants

Sixty-nine healthy students from Semnan University of Medical Sciences were recruited using a simple non-probability sampling method. This sample size allows detecting the effect of M1 and cerebellar a-tDCS (power of 85%) with 95% confidence interval (CI). Based on consideration of inclusion and exclusion criteria, 10 volunteers were excluded and only 59 healthy individuals were participated in the study (43 women and 16 men with mean age of 23.16 years). Using sequences of random numbers, participants were randomly divided into three groups: M1, cerebellar and sham-a-tDCS groups. Fig. 1 shows the flowchart of eligibility assessment throughout the study. Participants were included if they were 18–35 years and had no history of neurological diseases.

![Flowchart](image)
or musculoskeletal disorders. Participants with severe perceptual and memory problems assessed by Mini Mental Status Examination (MMSE) scores of less than 21; having a history of any neurological disease, especially Parkinson or Alzheimer’s, brain surgery, visual or auditory problems, brain tumor, having intracranial metal implantation, medications for any neurological condition, or having any musculoskeletal or rheumatoid condition affecting range of motion in upper extremity were excluded from the study. All participants were right-handed, as determined by the Edinburgh Handedness Inventory (10 item version) (Light and Singh, 1987). All participants were interviewed and examined by a physician prior to entering to the study and provided written, informed consent. This trial study met the criteria in CONSORT checklist.

2.2. Study design

The design of study was parallel, randomized, double blinded, sham-controlled study. Groups of participants (n = 20 in two groups and n = 19 in the third group) received a-tDCS under each of the three different experimental conditions in a random order: (1) serial response time test (SRTT) training + a-tDCS of M1, (2) SRTT training + a-tDCS of cerebellum and, (3) SRTT training + sham TDCS. RT and the number of errors were measured before, 35 min and 48 h after completion of the experimental conditions (Fig. 2).

This study was conducted during the second half 2015 in the Neuromuscular Rehabilitation Research Center, Department of Physiotherapy, Semnan University of Medical Sciences. The study was approved by Human Ethics Committee at the Semnan University of Medical Sciences, Semnan, Iran, which is aligned with declaration of Helsinki. The study was registered as a clinical trial study on Iranian Registry of Clinical Trials (The registration number: IRCT2015030221294N1, www.irct.ir) after the enrolment of all participants.

3. Tool for induction and assessment of motor learning

For induction and assessment of motor learning, a custom designed software program known as Color Matching Test (CMT) was used to emulate a SRTT condition with second-order structural pattern. SRTT is one of the most common methods to assess implicit motor learning that included both motor and cognitive components (Nissen and Bullemer, 1987). In CMT software, a square repeatedly appears in the center of a computer screen which each time may have a different color. These colors are yellow, red, green, and blue and each of them is assigned to a specific key on the keyboard which include left shift, C, M and right shift keys, respectively. By pressing the correct key with the index finger of the right hand, the next colored square would appear. The main training task includes 8 blocks with one-minute rest between the training blocks. Presentation of colors were sequenced in all blocks except in blocks 5 and 6 which the colors are presented in random. Each sequenced block included 10 trials and each trial possesses 8 color cues in a particular sequence (i.e. YRGYBGY...YRGYBGY) (Stagg et al., 2011). Each random block is also included 10 trials but the color cues are presented randomly (i.e. RBGYBRYG...GBRYYBGR).

Prior to the test, the participants became familiar with the instruction and the rules of the training. For assessment of online learning, eight blocks of the task were used in experimental condition. The average of the RT and the number of errors for first and last blocks were used for analysis of online learning. For assessment of learning effects, two blocks of the sequenced task were used before, 35 min and 48 h after completion of all experimental conditions. The test enables us to assess the RT and the number of errors in each block. The average of these two blocks at baseline and two retention time points were used for further analysis of short-term and long-term offline learning.
Fig. 3. Electrode montage for a-tDCS of M1 and cerebellum. (a) For a-tDCS of M1, active electrode was located over left M1 and the returning electrode was located over the right contralateral supraorbital area. (b) For a-tDCS of cerebellum, active electrode was placed over ipsilateral cerebellum (1 cm below inion of occipital bone and 1 cm medial to mastoid process) and the returning electrode was placed over right arm.

4. Transcranial direct current stimulation

In M1 a-tDCS group, an active saline-soaked surface sponge electrode was positioned over the M1 (C3, International 10–20 system) and a returning electrode was located over the right contralateral supraorbital area (Nitsche et al., 2003; Kang and Paik, 2011) (Fig. 3a). In cerebellar a-tDCS group, the active anode electrode was placed over ipsilateral cerebellum (1 cm below inion of occipital bone and 1 cm medial to mastoid process). The returning electrode was placed over right arm (Ferrucci et al., 2013) (Fig. 3b). The size of active and returning electrodes of tDCS that used on M1 or cerebellum was 5 cm × 5 cm. The tDCS device (tDCS Brain Stimulation Device – ApeX Type A, USA Model, China) for cerebellar and M1 a-tDCS groups was set to deliver 2 mA direct current for 20 min, in which the first and last 10 s were adjusted gradually, to minimize the side effects (Nitsche and Paulus, 2000; Galea et al., 2009; Brunoni et al., 2011). The electrodes were fixed with two horizontal and perpendicular straps. In the sham group, the electrodes were randomly placed in the same positions as for M1 or cerebellar a-tDCS montages, but the stimulator was turned off after 1 min of stimulation.

5. Experimental procedures

Participants were asked to sit in front of a computer monitor and press the relevant key as soon as they see a square in the monitor. With the beginning of the main test, participants also received intervention with a-tDCS (Hardwick and Celnik, 2014). The previous studies indicated that simultaneous application of a-tDCS and motor tasks can effectively enhance motor behavior (Nitsche et al., 2003; Ehsani et al., 2015; Kuo et al., 2008). There were 8 blocks in the main test. Blocks 5 and 6 had a random pattern and the others appeared with ordered pattern. Two retention tests included two ordered blocks were given 35 min and two days later to check out the mandatory of the first test performance improvement and motor learning following a-tDCS. If participants recognized the order of sequences, their data were omitted from data analysis. To determine baseline data in each participant, a pretest with 2 ordered blocks was given before the main simultaneous a-tDCS/training intervention.

Participants were blinded to the condition of a-tDCS (sham or active). Fig. 1 shows the process of the clinical trial through various stages (Enrollment, Allocation, Follow-up, and Analysis). Two blind assessors to study’s groups were involved in this study, one for administering of a-tDCS during execution stage and another for assessing outcome measures after data collection stage.

6. Assessment of the side effects

To assess side or adverse effects, all participants were asked to complete a questionnaire during and after a-tDCS intervention. The questionnaire included rating scales; numeric analog scales (NAS) (e.g., 0 = no tingling to 10 = worst tingling imaginable); to determine the presence and severity of side effects such as itching, tingling, burning sensations under electrodes (George and Aston-Jones, 2010; Nitsche et al., 2008) and also evaluate adverse effects such as headache and pain during and after stimulation.

7. Operational definitions

The RT that obtained from the mean of time for completion of each block and the task errors that obtained from the mean of errors for each block were recorded as the main variables to assess motor learning. Online learning is the learning, which happens during training. Any decrease in the RT at the block 10 (T10) compared to the block 3 (T3) or reduction the errors of block 10 (Error10) than block 3 (Error3) were considered as online learning. Unlike online learning, short term and long term offline learning was defined as the learning, which happened after the completion of the training (35 min and 48 h post intervention, respectively). In this case, any decrease in the RT of block 12 (T12) than block 2 (T2) or reduction the errors of block 12 (Error12) than block 2 (Error2) were considered as short-term offline learning. Likewise, any decrease in the RT of block 14 (T14) than block 2 (T2) or reduction the errors of block 14 (Error14) than block 2 (Error2) were considered as long-term offline learning.

8. Data analysis

The data were blindly analyzed using SPSS software version 22. Kolmogorov–Smirnov test was conducted to evaluate the
normality of distribution for tested variables. Normal distribution was observed for all variables in all groups. A one-way ANOVA was also carried out to test lack of difference in the baseline values in the three stimulation sites. To assess the main effects of group (cerebellar, M1 and sham a-tDCS), time (T2, T3, T10, T12 and T14) and their interactions on the RT, a two-way repeated measure ANOVA was carried out. Similarly, a two-way repeated measures ANOVA was also used to evaluate the errors during test and retention tests among groups. In case of any significant main or interaction effect, post hoc tests with Bonferroni corrections were carried out to assess whether the baseline value of RT and error points in each group were differed significantly from post-intervention. Also, an independent sample t-test using Bonferroni correction was applied to evaluate significant differences of online, offline learning between groups. Type I error (α) was set at .05 and the power of tests was considered 0.85.

9. Results

9.1. The effect of a-tDCS on RT

Demographic details and baseline data for the participants in three groups are presented in Table 1. There were no statistically significant differences in age, gender, Mini Mental Examination (MMSE), baseline RT and errors (P > 0.05) among groups. The mean of RT and error number of essential blocks for three groups is shown in Table 2. Table 3 shows the results of a mixed-model repeated measure ANOVA. The between-subjects main effect of groups was significant (P < 0.05), which indicates differences in the learning among stimulation groups. The within-subjects main effect of time was also significant (P < 0.01), which indicates significant differences between degrees of learning during different time points (i.e. block 2, 3, 10, 12 and 14) (see Fig. 4). ANOVA also shows significant interaction effect between group and time (P < 0.01) which indicates significant differences among groups at some time points. Post hoc analysis using Bonferroni correction indicates significant RT changes between T2 and T10, between T2 and T12, first retention follow-up and between T2 and T14, second retention follow-up (48 h) in all three groups (Table 4). Moreover, Fig. 5(b) and (c) shows significant differences in short-term and long-term offline learning between the groups that received intervention with a-tDCS and sham-control group. However, there were not significant differences in online learning among groups (P > 0.05) (Fig. 5a). Also, the post hoc analysis revealed that there were no significant differences in online learning among cerebellar a-tDCS and M1 a-tDCS groups (P > 0.05). In addition, Fig. 5b indicates that short-term offline learning (RT) was significantly increased in M1 a-tDCS as compared to sham-control group (P = 0.023).

9.2. The effect of a-tDCS on number of errors

Moreover, the study also assessed the number of errors within each block and indicated significant within and between-subject main effects (P < 0.01) (Table 3). ANOVA also shows significant interaction effect between group and time points (P < 0.01) which
indicates significant differences among the groups at some time points. Table 4 shows significant errors reduction between Error2 and Error12, short-term offline learning and between Error5 and Error14, long-term offline learning in all three groups, while there are no significant errors reduction between Error3 and Error10 in M1 a-tDCS and sham-control groups. The results of independent t-test showed there was no significant difference in online error reduction among M1 a-tDCS and sham-control groups (P=0.37), while online error reduction was increased in cerebellar a-tDCS as compared to sham-control group (P=0.004) (see Fig. 5a). In addition, Fig. 5(b) and (c) shows significant differences in short-term and long-term (48 h) offline error reduction between groups that received intervention with a-tDCS and sham-control group (P<0.01), while there were not significant differences between cerebellar a-tDCS and M1 a-tDCS groups (P>0.05).

10. Safety and side effects of a-tDCS

All participants tolerated the applied currents very well with minimal adverse or side effects of the applied currents. Reported side effects (means ± SEM) under the anode and cathode for each group were summarized in Table 5. Itching is a side effect of a-tDCS, which was reported by most participants of study. Participants did not report any side effects after the end of stimulation. In addition, there were no reports of burning sensations, or pain by participants during or after stimulation.

11. Discussion

The results in current study indicate significant differences in short-term and long-term offline learning between the a-tDCS groups and sham tDCS group. The aim of the current study was to compare the effects of M1 and cerebellar a-tDCS on the RT and number of errors as two main parameters during learning. Findings revealed that a-tDCS application over both M1 and cerebellar regions similarly increased long-term offline learning in healthy individuals, while cerebellar a-tDCS had more effect on online learning (evidenced by reduction in number of errors) and M1 a-tDCS had more effect on short-term offline learning (evidenced by reduction in RT).

We hypothesized that cerebellar a-tDCS compared to stimulation of M1 induces more profound effect on online learning. The findings of study support this hypothesis. The findings indicated that although cerebellar a-tDCS produced similar online learning as
Fig. 5. (a) The comparison of online learning (changes in response time and errors number between blocks 3 and 10) (mean differences ± SEM) among groups, (b) the comparison of short-term offline learning (changes in response time and errors number between blocks 2 and 12) (mean differences ± SEM) among groups, (c) the comparison of long-term offline learning (changes in response time and errors number between blocks 2, 14) (mean differences ± SEM) among groups; * indicates significance difference. SEM stands for standard error of measurement.
Table 5

<table>
<thead>
<tr>
<th></th>
<th>Anode electrode</th>
<th>Cathode electrode</th>
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<tbody>
<tr>
<td></td>
<td>Cerebellar a-tDCS</td>
<td>M1 tDCS</td>
</tr>
<tr>
<td>Tingling sensation</td>
<td>Beginning</td>
<td>5.2 ± 0.32</td>
</tr>
<tr>
<td></td>
<td>Middle</td>
<td>3.8 ± 0.21</td>
</tr>
<tr>
<td></td>
<td>End</td>
<td>1.9 ± 0.17</td>
</tr>
<tr>
<td>Itching sensation</td>
<td>Beginning</td>
<td>3.7 ± 0.14</td>
</tr>
<tr>
<td></td>
<td>Middle</td>
<td>2.2 ± 0.21</td>
</tr>
<tr>
<td></td>
<td>End</td>
<td>1.7 ± 0.19</td>
</tr>
<tr>
<td>Burning sensation</td>
<td>Beginning</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Middle</td>
<td>–</td>
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<td></td>
<td>End</td>
<td>–</td>
</tr>
<tr>
<td>Not tolerated</td>
<td>Beginning</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Middle</td>
<td>–</td>
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Numeric Analogue Scale (NAS): 0 is rated as no sensation and 10 rated as the worst sensation imaginable; was used to rate the values of side effects. The participants reported their sensations under both active (anode) and reference (cathode) electrodes during three phases of tDCS stimulation of primary motor cortex (M1), cerebellum, and sham tDCS: beginning (0–7 min of stimulation), middle (7–14 min of stimulation), and end (14–20 min of stimulation). Scores are reported as mean ± SEM (SEM: standard error of measurement).

compared to M1 a-tDCS, there was significant difference between cerebellar a-tDCS and sham tDCS group in error reduction during online training. The findings of this study are supported by the findings by Galea et al. (2011). They found that compared to a-tDCS of M1 and sham stimulation, cerebellar tDCS induces more online learning by reduction of RT and decrease in number of errors (Galea et al., 2011). Galea et al. (2011) also reported that the cerebellar a-tDCS induces significant largest reduction of error during adaptation phase. These findings are also supported by findings of the other studies, which reported reduction of error numbers following application of a-tDCS over the cerebellum (Herzfeld et al., 2014; Hardwick and Celnik, 2014; Kitazawa et al., 1998; Tseng et al., 2007). It seems that cerebellar a-tDCS can increase cerebellar excitability during training by enhancing the spatial realignment of SRT task in form of online and finally lead to faster movements with reduction of error numbers (Hardwick and Celnik, 2014; Galea et al., 2011).

In the current study, M1 a-tDCS group did not show greater online error reduction as compared to sham-control group. The findings of the Galea et al. (2011) study also indicated that reduction of error numbers following application of M1 a-tDCS was not difference with sham/no tDCS immediately after training. It appears that M1 a-tDCS technique cannot modulate the cortical transmitter system immediately and does not affect online learning (Floyer-Lea et al., 2006).

It was also hypothesized that, compared to stimulation of M1, cerebellar a-tDCS induces more profound effects on reduction of RT and error numbers. The findings in the current study did not support this hypothesis. Long-term offline learning was similarly increased by a-tDCS of both M1 and cerebellum (P > 0.05). Moreover, the findings of the current study indicated that M1 a-tDCS induces more short-term offline learning effect (evidenced by reduction of RT) as compared to sham/no tDCS, while this significant short-term effect was not observed between cerebellar and sham/no tDCS groups. Most of the previous studies investigating efficiency of M1 a-tDCS on motor skill acquisition indicated lasting effect of M1 a-tDCS on improvement of motor function (Boggio et al., 2006; Hummel et al., 2005; Reis et al., 2009; Orban de Xivry and Shadmehr, 2014). In addition, Galea et al. (2011) study also indicated that reduction of error numbers following application of M1 a-tDCS was significantly increased 10-min after training. It seems that M1 a-tDCS may consolidate motor learning by prolonging skill acquisition through an offline effect and play a critical role in retention of acquired skills (Reis et al., 2009; Galea et al., 2011; Kang and Paik, 2011). To the best of our knowledge, Galea et al. (2011) and Herzfeld et al. (2014) are the only studies that compared M1 and cerebellar a-tDCS on online and short-term offline motor learning (Galea et al., 2011; Herzfeld et al., 2014), while the current study assessed the lasting of the effects up to 48 h after the completion of the intervention. Galea et al. (2011) study indicated greater online effect of cerebellar a-tDCS and short-term offline effect of M1 a-tDCS on the errors reduction during visuomotor task in young healthy individuals. The current study confirmed this study and also revealed lasting effect of both M1 and cerebellar a-tDCS interventions on skill acquisition. In contrast, Herzfeld et al. (2014) assessed lasting of the effects up to 24 h after the completion of the stimulation and observed only cerebellar a-tDCS had lasting effect on motor memory. They indicated that retention was not improved by M1 a-tDCS (Herzfeld et al., 2014). It appears that M1 a-tDCS not only improves the learning of motor tasks but also enhances learning of cognitive visuomotor task (Reis et al., 2009; Galea et al., 2011). The discrepancy between the findings of these studies may be caused by different tasks and other methodological differences between these studies (Galea et al., 2011; Herzfeld et al., 2014). This indicates necessity of well controlled future studies to address these discrepancies.

Findings of the current study indirectly indicated that application of a-tDCS over the cerebellum and M1 during a visuomotor training task increases excitability of the involved neurons and improves motor learning. In this regard, majority of previous studies reported that application of tDCS prior to the training task could not significantly improve the rate of learning (Kuo et al., 2008; Stagg et al., 2011). This indicates that it may be better to have concurrent application of tDCS and training. The finding in current study supports this concurrent application. In addition, the current study also confirmed the findings of previous studies which tDCS enhancement of the motor learning is polarity dependent (Nitsche and Paulus, 2000; Stagg et al., 2011). Anodal tDCS could increase the rate of motor sequence learning, while cathodal tDCS induces opposite effects (Nitsche and Paulus, 2000; Stagg et al., 2011; Orban de Xivry and Shadmehr, 2014).

Literature indicates functional connectivity between M1 and cerebellum during learning processing of visuomotor tasks (Nitsche et al., 2004). This indicates that, both M1 and cerebellum have a key role in motor learning. Therefore, a-tDCS of either site may improve this connectivity which may lead to improved motor learning in healthy individuals (Celnik, 2014; Nitsche et al., 2004). a-tDCS of M1 or cerebellum as well as the active training may suppresses the
inhibitory system by decreasing activity of gamma-aminobutyric acid (GABA)-ergic system. This may generally affect the motor system to improve offline motor learning (Nitsche et al., 2004). In line with this finding, Hess et al. (1996) also reported that a decrease in activity of GABAergic system is required for long-term potentiation in the motor cortex (Hess et al., 1996). In addition, it seems that a-tDCS over both M1 and cerebellum increases firing rate of neurons and strengthen the newly formed associations among neurons which can affect neural networks and consolidation of sequence learning task (Nitsche et al., 2003; Orban de Xivry and Shadmehr, 2014). Bindman et al. (1962) also indicated that excitability of neurons was increased during and for several hours after anodal polarization. Accordingly, application of one session of M1 and cerebellar a-tDCS can engrave new firing patterns in memory and facilitate offline motor learning processing that indicated in the current study.

11.1. Safety and side effects of a-tDCS

The results of the current study suggest that application of a-tDCS over both M1 and cerebellum is safe and leads to minimal side effects with no adverse effect such as seizure, headache, or nausea in healthy individuals. General discomfort (itching and/or tingling) was the most reported side effects of active and sham tDCS by participants.

11.2. Limitations of the study

Several limitations in this study should be noted. First, the findings in this study should be considered based on these limitations. The participants were healthy young adults (<35 years), therefore it is not possible to extrapolate the results to older adults or patients with pathological conditions. Older adults may respond differently to cerebellar or M1 a-tDCS. Second, most of participants were females, which limit the extrapolation of these findings to the male populations. Third, large 5 cm × 5 cm electrodes were used in this study. Nearby cortical regions may have also stimulated by these less focused electrodes. This might affect the findings of the current study.

Since Color Matching Task is a cognitive motor task, M1 anodal stimulation modulates motor function, and frontal cathodal stimulation may also modulate cognitive function of task in the “M1 stimulation” setting. However, there was no similar condition for the ‘cerebellar stimulation” setting. This different setting in M1 and cerebellar a-tDCS may make the limitation for comparison of M1 and cerebellar a-tDCS effects on motor learning.

11.3. Suggestions for future research

Our study did not assess the effects of multiple session application of a-tDCS. Further studies are required to fully characterize the effects of concurrent application of a-tDCS and SRTT on motor learning. In the current study, the effect of a-tDCS of M1 and cerebellum with SRT task training was assessed. Further studies are also recommended to investigate if a-tDCS of M1 and cerebellum has different or similar effects on motor learning during more challenging motor training task. In addition, further studies are recommended to conduct on older population to investigate the priming effect of a-tDCS on older population. Investigation of gender effect is also important, which requires further attention. Moreover, using more localized electrodes in further studies is also recommended in future studies. The task of the current study was including both motor and cognitive functions. Further studies with using simple motor task are also recommended to compare specifically M1 and cerebellar a-tDCS effects on motor learning.

12. Conclusion

The results indicate that compared to sham stimulation, a-tDCS of cerebellum enhances online motor learning, while a-tDCS of M1 is more effective in induction of short-term offline motor learning. The current study has shown for the first time that both M1 and cerebellar a-tDCS can be used as effective techniques for improvement of offline learning in healthy individuals. As both primary motor cortex and cerebellum have key role in processing of implicit motor learning, the application of a-tDCS over both M1 and cerebellum may similarly induce changes in motor learning which may last up to 48 h in healthy individuals.

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References


