Noninvasive brain stimulation over M1 and DLPFC cortex enhances the learning of bimanual isometric force control

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ABSTRACT

Motor learning plays an important role in upper-limb function and the recovery of lost functionality. This study aimed to investigate the relative impact of transcranial direct current stimulation (tDCS) on learning in relation to the left primary motor cortex (M1) and left dorsolateral prefrontal cortex (DLPFC) during bimanual isometric force-control tasks performed with both hands under different task constraints. In a single-blind cross-over design, 20 right-handed participants were randomly assigned to either the M1 group ($n = 10$; mean age, 22.90 ± 1.66 years, mean ± standard deviation) or the DLPFC group ($n = 10$; mean age, 23.20 ± 1.54 years). Each participant received 30 min of tDCS (anodal or sham, applied randomly in two experiments) while performing the bimanual force control tasks. Anodal tDCS of the M1 improved the accuracy of maintenance and rhythmic alteration of force tasks, while anodal tDCS of the DLPFC improved only the maintenance of the force control tasks compared with sham tDCS. Hence, tDCS over the left M1 and DLPFC has a beneficial effect on the learning of bimanual force control.

1. Introduction

Motor learning occurs when movements are performed effortlessly after one or more practice sessions (Willingham, 1998) aimed at improving performance (Wolpert, Ghahramani, & Flanagan, 2001). It plays a particularly important role in the normal functioning and rehabilitation of the upper limbs (Sigrist, Rauter, Riener, & Wolf, 2013). Motor learning has been widely studied (Boudreau, Hennings, Svensson, Sessle, & Arendt-Nielsen, 2010; de Camargo Barros, Tani, & Corrêa, 2017), and is only achievable through practice (Schmidt & Lee, 1999). Strategies to enhance the motor learning process that do not involve practice, which is often time consuming and requires considerable effort, are of great scientific and practical significance (Lieberman & Breazeal, 2007; Reis & Fritsch, 2011; Sigrist et al., 2013).

Since changes in the cortical network, especially those related to motor and cognitive brain areas (Ungerleider, Doyon, & Karni, 2002), are associated with motor learning, transcranial direct current stimulation (tDCS) has been used to promote the learning process via modulating cortical excitability. Previous studies that aimed to uncover the underlying mechanism of tDCS have shown that anodal tDCS induced similar intra-cortical changes in the motor learning process. At a physiological level, these studies have demonstrated that both anodal tDCS and motor learning are accompanied by a reduction of the concentrations of the inhibitory neurotransmitter γ-aminobutyric acid (Kim, Stephenson, Morris, & Jackson, 2014; Stagg, Bachtiar, & Johansen-Berg, 2011), which

suggests that anodal tDCS could promote learning processing similar to natural learning via neurochemicals. Among the target brain areas of studies investigating the beneficial effect of tDCS on motor learning, the primary motor cortex (M1) (De Xivry & Shadmehr, 2014; Reis et al., 2008) is the most studied. Previous studies have provided evidence that anodal tDCS of the M1 could improve the learning process of manual tasks in healthy individuals (Fan, Voisin, Milot, Higgins, & Boudrias, 2017; Furuya, Nitsche, Paulus, & Altenmüller, 2013; Nitsche et al., 2003; Reis et al., 2009; Schambra et al., 2011). However, these studies only investigated unimanual tasks (Fan et al., 2017; Nitsche et al., 2003; Reis et al., 2009; Schambra et al., 2011) or bimanual movement tasks (Furuya et al., 2013); hence, the effect of tDCS on bimanual force control remains unknown.

Considering that bimanual force control is common during activities of daily living and constitutes an indicator of functional recovery of patients after stroke (Kang & Cauraugh, 2014; Lodha et al. 2012) , it is of interest to investigate whether tDCS could promote learning of bimanual force control. Previous evidence has shown that the amplitude of bimanual actions should activate the dorsolateral prefrontal cortex (DLPFC) anterior cingulate cortex supramarginal network, which is involved in executive functions (Wenderoth, Debaere, Sunaert, & Swinnen, 2005); additionally, modulation of the interhemispheric coupling of the sensorimotor cortices occurs during bimanual learning (Swinnen, 2002). Other studies have demonstrated that the left M1 and left DLPFC are associated with the learning of bimanual tasks (Beets et al., 2014; Neva, Vesia, Singh, & Staines, 2014) and that both the left M1 (Kami et al., 1995) and the left DLPFC (Beets et al., 2014) are involved in the acquisition process of motor learning. However, the DLPFC has been mostly investigated in terms of cognitive tasks in tDCS studies; as such, its effects on motor control remain largely unknown. A recent study showed no enhancement of learning during a complex bimanual movement task under tDCS over the left M1 and DLPFC (Vancleef, Meesen, Swinnen, & Fujiyama, 2016); however, another study showed beneficial learning effects of tDCS on a unimanual grip force task (Fan et al., 2017). As the tDCS effect is task specific (Filmer, Dux, & Mattingley, 2014; Saucedo, Zhang, Swinnen, Meesen, & Wenderoth, 2013) and differs as a function of the prevailing task constraints, the relative impact of the left M1 and DLPFC on bimanual force control remains a topic of investigation. Indeed, evidence from patients is promising; however, considering that no prior studies have investigated the learning effect of tDCS among patients with bimanual force control deficits, it is necessary to firstly evaluate its safety and efficacy in participants without a disability.

Here, we aimed to investigate the relative impact of tDCS over the left M1 and left DLPFC on motor learning in bimanual force control. Based on previous evidence indicating that M1 and DLPFC are involved differentially in bimanual tasks and that the tDCS effect is task-specific, we hypothesized that the effect of tDCS on the learning of bimanual isometric force control would differ among brain areas and task constraints. To test this hypothesis, we applied tDCS during different bimanual force control tasks and evaluated the learning effect by analyzing the accuracy and coordination of the bimanual force output.

2. Methods

2.1. Subjects

Twenty healthy young adults (four women; mean age, 23 ± 1.6 years; mean ± standard deviation) participated in the study. The exclusion criteria were any known sensorimotor or neurological deficits, metal objects in the head, previous head injury, pregnancy, or any other serious medical condition. The study was approved by the institutional review board of Korea University and conducted in accordance with the principles of the Helsinki Declaration; the aim of the study was explained to all participants and they provided informed consent to participate. Additionally, all subjects were evaluated with their dominant hand using the Edinburgh Handedness Inventory (Oldfield, 1971).

2.2. Design and procedure

This was a randomized single-blind cross-over study. Twenty randomization numbers were generated; five were matched with 1 (anodal tDCS of M1), five with 2 (sham tDCS of M1), five with 3 (anodal tDCS of the DLPFC), and five with 4 (sham tDCS of the DLPFC) for the first visit following a pseudo-counterbalanced order (Matsuo et al., 2011). Each of the random numbers was printed and placed in an opaque envelope, and each subject chose one envelope at the first experimental session in the order of recruitment. The randomization and the tDCS type set-up was conducted by JH. The subject was blinded to the tDCS type by the random application of the actual and sham tDCS. Each subject participated in two experimental sessions on two separate days with a washout period of 1–2 weeks. A schematic representation of the experimental procedure is shown in Fig. 1a.

During each experimental session, the pre-bimanual maximum voluntary force (BMVF) was measured first. Thereafter, under the application of 30 of minutes of tDCS (type according to the random allocation), the participants randomly performed four bimanual force-matching (BFM) tasks. After the BFM tasks, the post BMVF was measured; pain during stimulation was also measured using the visual analogue scale (VAS). At the end of the second experimental session, the subjects were asked to determine whether they had received an anodal stimulation or sham stimulation during each experiment as the result of stimulation sensation.

2.3. Apparatus

2.3.1. Isometric force recording

Two rigid Styrofoam™ boards were used to support and fix the wrists and forearms. The position of the sensors could be adjusted in the forward-backward and medial-lateral direction within a range of 30 mm and 60 mm respectively to fit the subjects' fingers. After comfortable positions of both hands were confirmed, the positions were marked and maintained during the test.
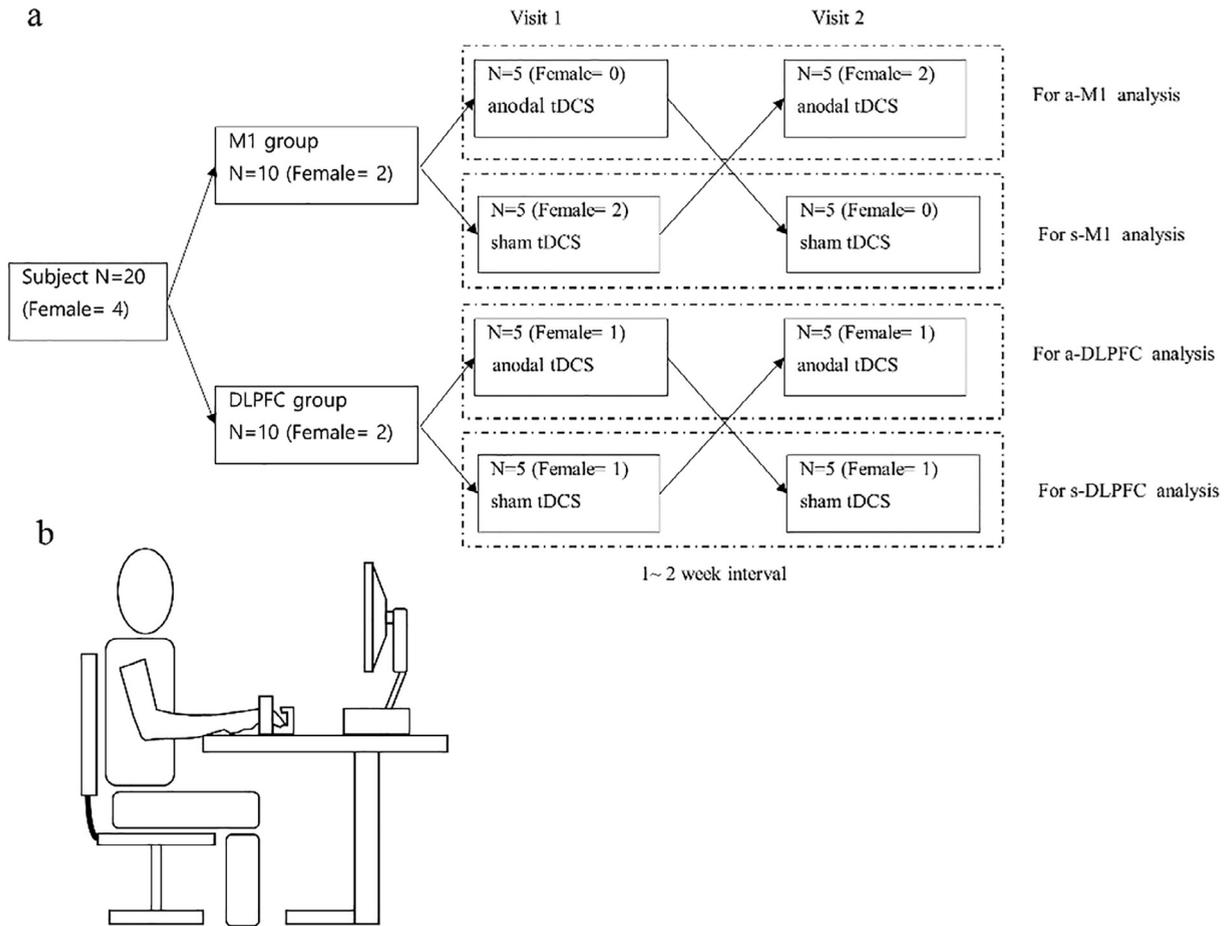
Fig. 1. Experimental design (a) and posture of the subjects during the experiment (b) a: Experimental procedure; b: Posture during experiment *tDCS, transcranial direct current stimulation; M1, primary motor cortex; DLPFC, dorsolateral prefrontal cortex.*

Analogue output signals from the sensors were processed using separate AC/DC conditioners (482C, PCB Piezoelectric, Inc., Depew, NY, USA). The system was operated in a DC-coupled mode, using the sensor's discharge time constant as established by the built-in microelectronic circuit within the sensor. A 16-bit A/D board (NI 9215; National Instruments, Austin, TX, USA) was used to digitize all of the signals at 1000 Hz. Details of the apparatus are described elsewhere (Kim, Kim, & Yoon, 2014).

The participants were seated comfortably at a distance of 70 cm in front of a 20-inch screen. Thereafter, the sensor was placed on each hand; with each hand maintained at 20° of wrist extension and 20° of metacarpophalangeal flexion, the interphalangeal joints were slightly flexed so that the hand could form a dome. These comfortable positions were marked and maintained throughout the experiment (Fig. 1b).

2.3.2. TDCS application

A battery driven tDCS (Ybrain Inc, Korea) device with an intensity of 2 mA and a conductive rubber electrode of $5 \times 5 \, cm^2$ for both the anodal and cathodal (current density, 0.08 mA/cm^2) electrodes, which were placed in 0.9% NaCl soaked sponges, was used. The center of the anodal electrode was placed over the left M1 (for the a-M1 and s-M1 groups) or left DLPFC (for the a-DLPFC and s-DLPFC groups). The left M1 was localized at C3, while the left DLPFC was localized at F3 according to the 10/20 international EEG placement (DaSilva, Volz, Bikson, & Fregni, 2011). Studies focusing on the tDCS effect on hand function chose C3 or C4 to represent M1 (Boggio et al., 2006; Hummel et al., 2010). Accordingly, since we were interested in hand function, we used the general M1 area. The center of the cathodal electrode was placed over the right supraorbital area which corresponds to Fp2. The electrodes were fixed on the head using an elastic bandage. In the anodal experimental groups (a-M1 and a-DLPFC), a 2-mA current was continued during the tasks for 30 min. In the sham experimental groups (s-M1 and s-DLPFC), the current was turned off after the 30 s ramp up phase to 2 mA programmed in the tDCS device, to induce a sensation similar to that of anodal stimulation but without a long-lasting effect.

2.4. Task

Pre-BMVF. Each subject was instructed to press both hands as hard as possible for 5 s and then relax without lifting the hands off
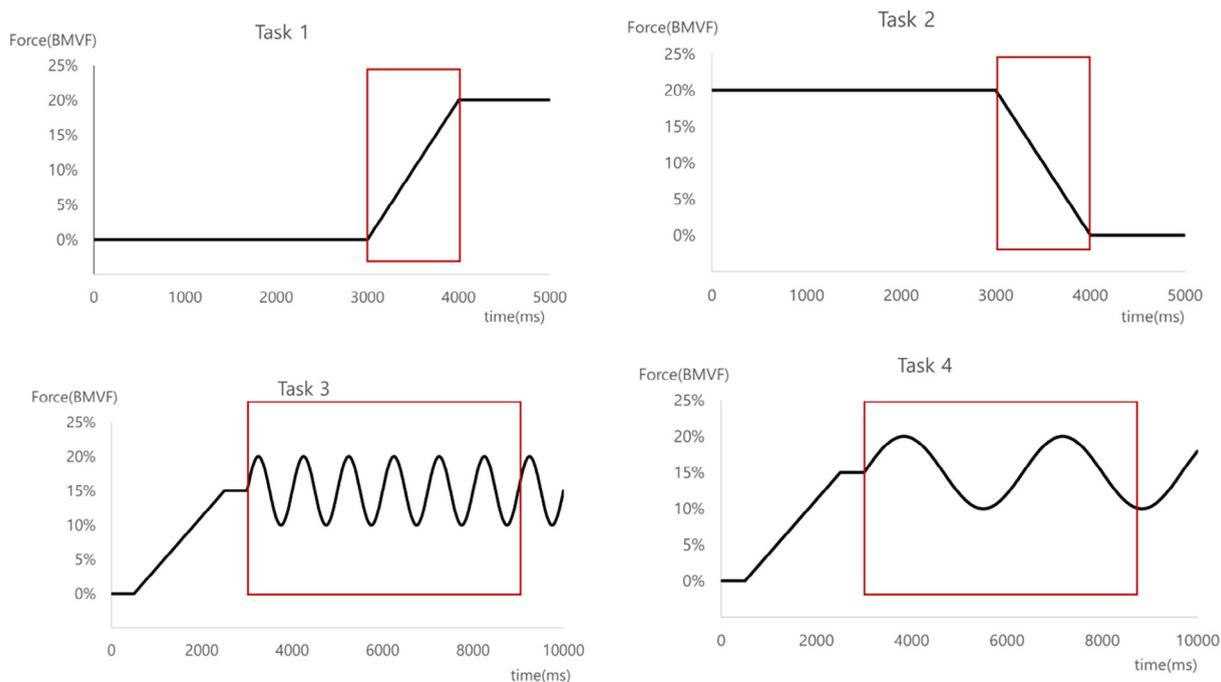
Fig. 2. Bimanual force matching tasks *BMVF, bimanual maximum voluntary force* *The red box indicated the period for analyse. Task 1: 1 s ramping up period (from 3 s to 4 s); task 2: 1 s ramping down period (from 3 s to 4 s); task 3: 6 s of 1 Hz sine wave period (from 3 s to 9 s); task 4: 6 s of 0.3 Hz sine wave period (from 3 s to 9 s). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

the sensors. During each trial, a visual representation of the force produced by the participant was shown in a horizontal bar on a computer screen, in order to motivate subjects to produce the BMVF at maximum effort (Jung & Hallbeck, 2004). Data were collected for 5 s. Three trials were performed consecutively with 30-s intervals to prevent fatigue. Prior to the trial, the subjects performed one practice trial. The mean value of the three trials was used for the BMVF.

BFM tasks. The BFM tasks consisted of four tasks. The force target levels used in the experiment were scaled to each subject's BMVF. The subjects were then instructed to press both hands to match the target force line (blue line) as accurately as possible with continuous visual feedback of the total bimanual force output (white line) on the screen. The task representations are shown in Fig. 2. Task 1 was a 5-s force matching task, which included a 3-s horizontal line at 0% BMVF, 1-s ramp up line to 20% BMVF, and 1-s horizontal line remaining at 20% BMVF. Task 2 was a 5-s force matching task, which included a 3-s horizontal line at 20% BMVF, 1-s ramp down line to 0% BMVF, and 1-s horizontal line remaining at 0% BMVF. Task 3 was a 10-s force matching task, which included a 3-s preparing line and 7-s for the 1 Hz sine wave with a force between 10% BMVF and 20% BMVF. Task 4 was similar to task 3, but with 7-s of a 0.3 Hz sine wave after a 3-s preparing line. According to the frequency, task 3 was a higher speed condition, while task 4 was a slower speed condition. Ten trials were performed consecutively for tasks 1 and 2, and 15 trials were performed consecutively for tasks 3 and 4 with a 20-s interval between each trial and a 90-s interval between each task to prevent fatigue. During tasks 1 and 2 participants had to focus on adjusting and maintaining forces to a certain target force level, while tasks 3 and 4 had them focus on rhythmically altering and controlling forces within a given period. Since a previous study (Kang & Cauraugh, 2015b) showed that bimanual force control deteriorated between 5% and 50% maximal voluntary force, we designed the four tasks within 5%-50% force range. The order of the tasks was randomized.

Post-BMVF. The same procedures as in the pre-BMVF were performed in the post-BMVF.

2.5. Data processing

Raw force data were acquired using LabView (LabView 2010, National Instruments) and analyzed using MatLab (R2008a, MathWorks, Inc.). These data were low-pass filtered using a fourth-order Butterworth filter with a cut-off frequency of 20 Hz (Kang & Cauraugh, 2014). The force data selected for analysis was as follows. Task 1: 1 s ramping up period (from 3 s to 4 s); task 2: 1 s ramping down period (from 3 s to 4 s); task 3: 6 s of 1 Hz sine wave period (from 3 s to 9 s); task 4: 6 s of 0.3 Hz sine wave period (from 3 s to 9 s). The initial 3 s and last 1 s of tasks 3 and 4 were removed from the analysis to eliminate transient effects.

The primary outcome was the accuracy of the bimanual force output, while the secondary outcome was the bimanual force coordination. To analyze the systematic deviations from the target force of tasks 3 and 4, a nonlinear curve fit was calculated for bimanual force output using the least squares method to find the best fit (Vieluf, Godde, Reuter, & Voelcker-Rehage, 2013).

2.5.1. Accuracy of force production

The force production accuracy was estimated using the root mean square error (RMSE). The RMSE indicates the average sum of the squared deviations of the force production relative to the target force. Thus, the accuracy increases as the RMSE decreases. The learning effect was tested using the mean value of the first and last three trials of RMSE result of each BFM task.

2.5.2. Bimanual force coordination

The degree of temporal coordination between the participant's hands was examined by calculating the cross-correlation of the force output by each hand. To minimize the DC bias according to a previous study (De Luca, LeFever, McCue, & Xenakis, 1982), the force data were filtered using a zero phase filter with a low cut-off frequency of 0.75 Hz. Time-series cross-correlation was used to investigate the temporally synchronizing of force signals produced by each hand; the value was computed with varying lag values from 0 to N-1 (N = total number of force data samples). Bimanual force coordination was quantified using the peak values (Lodha et al. 2012). Higher cross-correlation values indicated enhanced bimanual coordination. The learning effect was tested using the mean value of the first and last three trials of cross-coordination result of each BFM task.

2.5.3. Nonlinear curve fit

The four parameters (frequency, phase shift, amplitude, and intercept) in tasks 3 and 4 of each participant were set up as the target fitting parameters. The frequency and phase shift were spatial parameters, and the amplitude and intercept were temporal parameters. Thereafter, the difference in the values of the four parameters (Δ frequency, Δ phase shift, Δ amplitude, and Δ intercept), defined as individual parameters subtracted from the target parameters (the individualized parameters of tasks 3 and 4 of each subject), were analyzed (Vieluf et al., 2013). The learning effect was tested using the mean value of the first and last three trials result of each BFM task.

2.6. Statistical analysis

All results are reported as mean ± standard deviation. The Shapiro-Wilk test was used to examine whether the data were normally distributed. The stimulation sensation was analyzed using the chi-square test. The VAS scores among the different tDCS groups were analyzed using one-way analysis of variance (ANOVA). Differences between the pre- and post-BMVF values of each group were analyzed using the paired t-test.

Four groups (a-M1, s-M1, a-DLPFC and s-DLPFC), four tasks, and two levels (first and last three trials) were tested. A three-way mixed measures ($4 \times 4 \times 2$, group × task × level) ANOVA was used to detect inter- and intra-subject differences in the RMSE and coordination variables. For tasks 3 and 4, a three-way mixed measures ($4 \times 2 \times 2$, group × task × level) ANOVA was used to detect differences in the Δ frequency, Δ phase shift, Δ amplitude and Δ intercept. If sphericity was violated, Greenhouse Geisser's degree of freedom adjustment was applied. To conduct multiple comparisons, the Bonferroni post hoc test within the ANOVA was used. All η^2 values were partial. All data were analysed using SPSS version 21 (IBM Corporation, USA) with significance set at $p < 0.05$.

3. Results

Subjects' characteristics, experiment interval, stimulation sensation, VAS score, and BMVF are shown in Table 1. The other outcomes are shown in Tables 2 and 3 (descriptive result cf., Table 2; statistics cf., Table 3); the post-hoc analysis was conducted for test results involving a significant group × task × level interaction.

Table 1
Demographics of the subjects, experiment interval, stimulation sensation, VAS score, and BMVF.

	M1		DLPFC		p
Group characteristics					
Age (y)	22.90 ± 1.66		23.20 ± 1.54		0.68
Sex (F/M)	2/8		2/8		1.00
Height (cm)	175.20 ± 7.36		171.10 ± 6.65		0.20
Weight (kg)	69.30 ± 14.72		69.30 ± 7.98		1.00
Handedness (%)	0.77 ± 0.12		0.78 ± 0.14		0.96
Experiment interval (day)	9.6 ± 2.7		8.6 ± 2.5		0.40
Stimulation sensation (right/ wrong)	8/2		9/1		0.53
	anodal	sham	anodal	sham	
VAS score	2.12 ± 1.90	1.59 ± 1.77	2.46 ± 1.88	1.34 ± 1.07	0.45
BMVF (N)					
pre	94.39 ± 28.39	86.39 ± 25.82	108.19 ± 19.70	94.23 ± 16.33	–
post	81.77 ± 36.63	82.79 ± 31.26	118.11 ± 28.54	103.94 ± 20.09	–
p	0.78	0.92	0.39	0.74	

Values are shown as means ± standard deviations. VAS, visual analogue scale; BMVF, bimanual maximum voluntary force; M1, primary motor cortex; DLPFC, dorsolateral prefrontal cortex.

Table 2
Accuracy, coordination (four tasks), and deviation of the curve fit parameters (tasks 3 and 4) from the target sine wave [Δ frequency (F), Δ phase shift (S), Δ amplitude (A), and Δ intercept (Y)].

	a-M1		a-DLPFC		s-M1		s-DLPFC	
	first 3 trials	last 3 trials	first 3 trials	last 3 trials	first 3 trials	last 3 trials	first 3 trials	last 3 trials
RMSE								
Task 1	2.31 ± 1.17	2.11 ± 0.72	2.74 ± 0.65	2.13 ± 1.20	2.19 ± 1.00	2.02 ± 0.94	3.16 ± 1.06	3.13 ± 0.57
Task 2	4.38 ± 1.82	2.94 ± 1.65	5.18 ± 1.06	4.06 ± 0.87	4.76 ± 1.96	4.15 ± 1.56	6.15 ± 1.67	5.42 ± 1.08
Task 3	2.82 ± 1.25	2.19 ± 1.13	3.42 ± 0.95	3.29 ± 0.73	3.09 ± 1.45	2.88 ± 1.17	4.07 ± 1.13	3.82 ± 0.96
Task 4	2.38 ± 1.41	1.91 ± 1.35	2.91 ± 0.60	2.91 ± 0.62	2.58 ± 0.99	2.51 ± 1.03	3.61 ± 1.01	3.42 ± 0.97
Cross-correlation								
Task 1	0.48 ± 0.08	0.48 ± 0.08	0.51 ± 0.04	0.51 ± 0.04	0.47 ± 0.04	0.49 ± 0.02	0.51 ± 0.05	0.51 ± 0.04
Task 2	0.36 ± 0.06	0.41 ± 0.07	0.35 ± 0.05	0.39 ± 0.07	0.35 ± 0.06	0.40 ± 0.05	0.35 ± 0.05	0.37 ± 0.06
Task 3	0.22 ± 0.03	0.21 ± 0.04	0.23 ± 0.02	0.22 ± 0.04	0.23 ± 0.05	0.21 ± 0.04	0.24 ± 0.03	0.21 ± 0.04
Task 4	0.25 ± 0.03	0.24 ± 0.02	0.21 ± 0.02	0.24 ± 0.04	0.22 ± 0.02	0.22 ± 0.03	0.23 ± 0.03	0.22 ± 0.03
Curve fit result								
Task 3 ΔF (Hz)	−0.02 ± 0.01	−0.02 ± 0.02	−0.02 ± 0.02	−0.02 ± 0.02	−0.02 ± 0.01	−0.01 ± 0.01	−0.02 ± 0.01	−0.001 ± 0.01
ΔS (s)	−0.006 ± 0.003	−0.003 ± 0.004	−0.005 ± 0.004	−0.006 ± 0.006	−0.004 ± 0.002	−0.003 ± 0.002	−0.005 ± 0.002	0.001 ± 0.002
ΔA (N)	−0.59 ± 0.13	−0.43 ± 0.14	−0.41 ± 0.32	−0.39 ± 0.35	−0.64 ± 0.61	−0.53 ± 0.34	−0.49 ± 0.29	−0.72 ± 0.36
ΔY (N)	0.16 ± 0.07	0.11 ± 0.03	0.41 ± 0.49	0.20 ± 0.31	0.14 ± 0.33	0.06 ± 0.21	0.54 ± 0.56	0.38 ± 0.40
Task 4 ΔF (Hz)	−0.005 ± 0.005	−0.007 ± 0.003	0.005 ± 0.004	0.005 ± 0.006	−0.003 ± 0.007	−0.007 ± 0.004	−0.002 ± 0.003	−0.002 ± 0.006
ΔS (s)	−0.001 ± 0.001	−0.002 ± 0.00	−0.001 ± 0.001	0.001 ± 0.001	0.001 ± 0.001	−0.002 ± 0.001	0.001 ± 0.00	0.001 ± 0.001
ΔA (N)	−0.31 ± 0.16	−0.22 ± 0.05	−0.38 ± 0.38	−0.32 ± 0.12	−0.37 ± 0.26	0.29 ± 0.16	−0.45 ± 0.35	−0.48 ± 0.36
ΔY (N)	0.18 ± 0.09	0.11 ± 0.05	0.21 ± 0.44	0.17 ± 0.17	0.23 ± 0.36	0.15 ± 0.27	0.42 ± 0.63	0.36 ± 0.26

Values are shown as means ± standard deviations. M1, primary motor cortex; DLPFC, dorsolateral prefrontal cortex; RMSE, root mean square error.

Table 3

Three-way mixed measures ANOVA results of the accuracy, coordination (four tasks), and deviation of the curve fit parameters (tasks 3 and 4) from the target sine wave [Δ frequency (F), Δ phase shift (S), Δ amplitude (A), and Δ intercept (Y)].

Measure	group				task				level			
	F	df	p	η^2	F	df	p	η^2	F	df	p	η^2
RMSE	89.3	3	< 0.01	0.31	20.3	3	< 0.01	0.13	54.3	1	< 0.01	0.28
Cross-correlation	2.45	3	0.4	0.03	289.2	3	< 0.01	0.78	11.3	1	0.013	0.077
ΔF (Hz)	7.23	3	0.67	0.015	19.101	1	< 0.01	0.23	10.2	1	0.07	0.127
ΔS (s)	7.23	3	0.67	0.015	19.101	1	< 0.01	0.23	10.2	1	0.07	0.127
ΔA (N)	3.4	3	0.03	0.09	4.3	1	0.19	0.08	1.1	1	0.03	0.02
ΔY (N)	2.45	3	0.04	0.10	1.3	1	0.45	0.02	3.02	1	0.02	0.04

Measure	group × task				group × level				task × level			
	F	df	p	η^2	F	df	p	η^2	F	df	p	η^2
RMSE	10.1	3	< 0.01	0.13	1.91	3	< 0.01	0.25	6.77	9	0.04	0.18
Cross-correlation	1.8	9	0.069	0.056	0.88	3	0.8	0.077	7.95	3	< 0.01	0.15
ΔF (Hz)	5.3	3	0.31	0.015	5.56	3	0.23	0.19	23.04	1	< 0.01	0.25
ΔS (s)	5.3	3	0.31	0.015	5.56	3	0.23	0.19	23.04	1	< 0.01	0.25
ΔA (N)	3.2	3	0.02	0.08	2.12	3	0.04	0.08	0.05	1	0.81	0.01
ΔY (N)	2.1	3	0.10	0.013	1.44	3	0.02	0.058	0.01	1	0.58	0.02

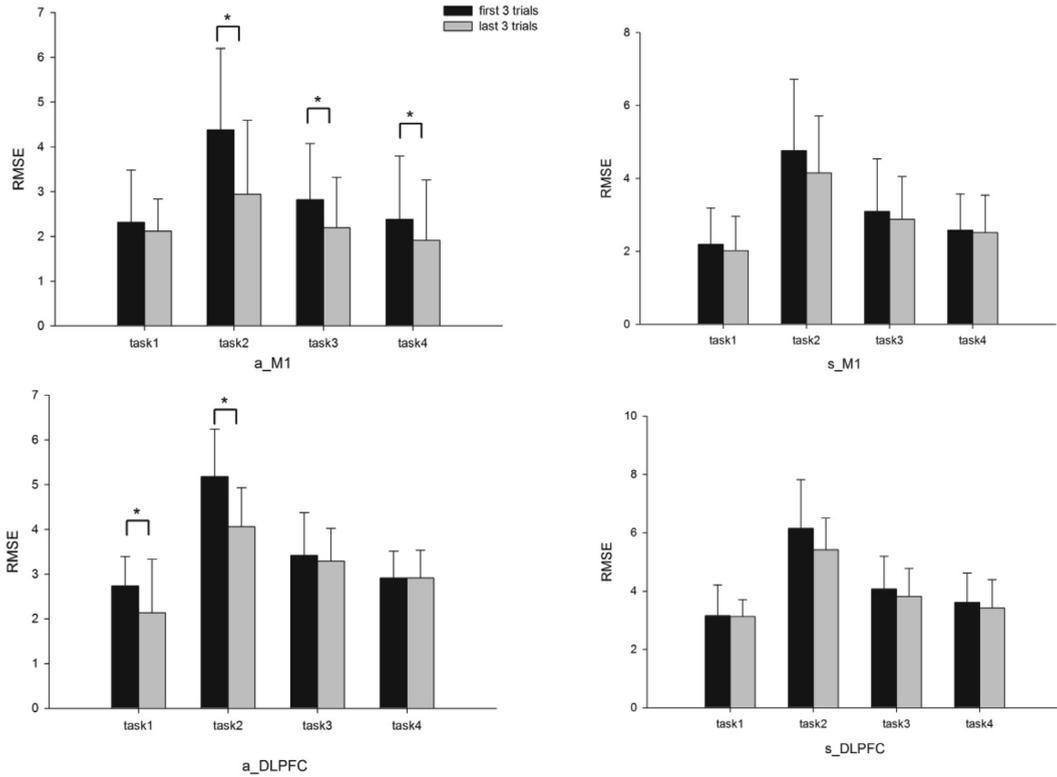| Measure	group × task × level			
	F	df	p	η^2
RMSE	0.2	9	0.04	0.30
Cross-correlation	0.46	9	0.04	0.03
ΔF (Hz)	4.95	3	0.06	0.17
ΔS (s)	4.95	3	0.06	0.17
ΔA (N)	2.61	3	0.03	0.03
ΔY (N)	2.68	3	0.04	0.02

RMSE, root mean square error.

Fig. 3. RMSE result *Post hoc result at $p < 0.05$.

3.1. Accuracy of force production

Main effects of group, task, and level were found; additionally, significant task × level, group × level, group × task, and group × task × level interactions were observed. The post-hoc analysis showed that the a-M1 group had a decreased RMSE in task 2 ($t = 3.1, p = 0.03$), task 3 ($t = 2.6, p = 0.04$), and task 4 ($t = 2.4, p = 0.045$), while the a-DLPFC group had a decreased RMSE in task 1 ($t = 3.0, p = 0.02$) and task 2 ($t = 2.8, p = 0.01$) (Fig. 3).

3.2. Bimanual force coordination

The cross-correlation values showed a main effect of task and level and a significant task × level interaction.

3.3. Curve fit parameters

The result showed a significant main effects of group and level, and significant group × level and group × task × level interactions for Δ amplitude and Δ intercept. The post-hoc analysis revealed that the amplitude was decreased in the a-M1 group in task 3 ($t = 3.7, p = 0.02$) and task 4 ($t = 5.8, p < 0.01$) and that the intercept was increased in task 3 ($t = 4.3, p < 0.01$) and task 4 ($t = 6.5, p < 0.01$) (Fig. 4).

4. Discussion

The aim of the present study was to investigate the effect of tDCS applied over the left M1 and DLPFC on the learning of bimanual isometric force control under different task constraints. The results showed that anodal tDCS over the M1 improved the accuracy of tasks 2–4, while anodal tDCS over the DLPFC improved the accuracy of tasks 1 and 2 compared with sham tDCS; the facilitated learning differed according to brain areas and task constraints.

Beneficial effects of anodal tDCS over the M1 were found with regard to the learning of bimanual force control, which varied over the different tasks. This result stands in contrast with that a previous study in which it was concluded that tDCS over the left M1 and left DLPFC had no beneficial effect on bimanual performance improvement during motor learning (Vancleef et al., 2016). This previous study involved a complex bimanual coordination task in which participants had to track a moving dot by rotating two dials with both hands simultaneously; no additive learning effects of anodal tDCS on acquisition or consolidation processes were observed. Because this movement task study had spatial constraints, the movement was coded by a population of neurons (Swinnen, 2002),
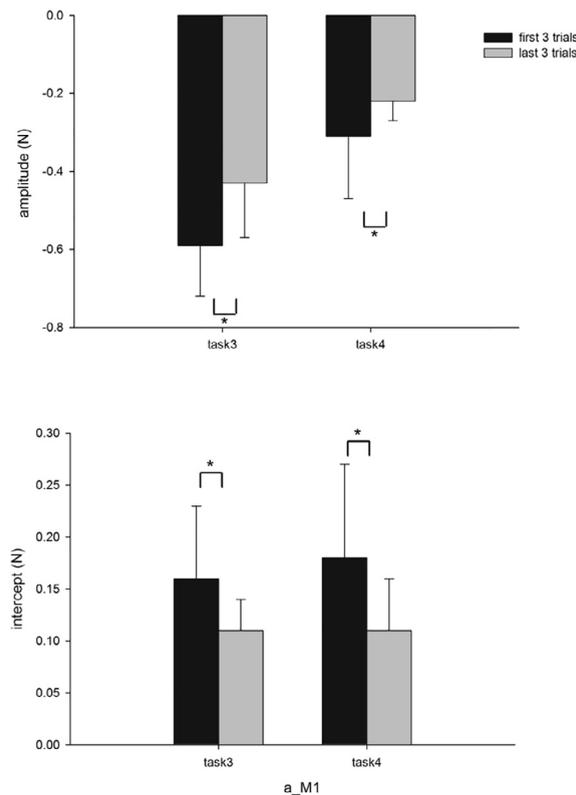
Fig. 4. Curve fit result *Post hoc result at $p < 0.05$.

which might not be sensitive to tDCS-induced changes. The present study showed that, in the a-M1 group, compared to the RMSE of the first and last three trials (Table 2), the accuracy of task 2 improved by 32.9%, which showed the greatest degree of improvement observed in the study. The performance accuracy of task 3 improved by 22.3%, while that of task 4 increased by 19.7%. Given that task 2 yielded the highest mean RMSE (4.38) on the first three trials, we can consider task 2 the most difficult task. Conversely, the mean RMSE on the first three trials of tasks 3 and 4 was 2.82 and 2.38, respectively. Task 1 yielded the lowest RMSE value on the first three trials (2.31). In view of these results, the higher the degree of difficulty during task performance, the greater the achieved improvement of performance accuracy under tDCS; this indicated that more difficult tasks allow greater improvements with tDCS support. While a-DLPFC significantly improved the accuracy in tasks 1 and 2, no significant difference was observed in tasks 3 and 4. The reason for this might be that tasks 3 and 4 were not difficult enough to require involvement of the cognitive function and attention supported by the DLPFC.

The four tDCS groups showed no difference in bimanual coordination. The correlation coefficient changes during tasks 2 and 3 showed a certain trend, but no significant difference. The correlation coefficient of task 2 in all four groups showed an increasing trend, whereas that of task 3 showed a decreasing trend. The increasing tendency of the correlation coefficients along with repeated trials in task 2 demonstrated that coordination contributes to the gradual decrease in bimanual force control (Kang & Cauraugh, 2015a). Conversely, the decreasing tendency of the correlation coefficients of task 3 illustrated that during rhythmically changed bimanual force control, less coordination between the hands might be required to achieve a more accurate performance.

Since RMSE could not detect the systematic deviations of the sine wave force matching tasks, we used the curve fit method to detect the spatial and temporal deviations responsible for the task performance. We found that a higher speed of the sine curve (task 3 with a 1-Hz frequency) led to a lower accuracy on the RMSE. As shown in Table 2, the RMSE value among all four groups of task 3 was higher than that of task 4, which means a lower accuracy of task 3 than task 4. This finding is in accordance with previously reported results (Sosnoff, Vaillancourt, & Newell, 2004). We further found that the spatial parameters (amplitude and intercept) of tasks 3 and 4 improved in the a-M1 group; the amplitude decreased from a high value to the target level, while the intercept increased from a low value to the target level. The improvements in the RMSE and spatial parameters could be explained by the enhanced accuracy under anodal tDCS on the M1. The temporal parameters (frequency, phase shift) matched the optimal timing of the target; we assume that this is caused by the high importance of the temporal control of visual force matching, which is coincides with the findings of a previous study (Vieluf et al., 2013) that investigated dominant hand precision grip during sine wave force tracking. The temporal parameters are first matched to ensure task performance. Aging also has an impact on the spatial parameters of sine wave tracking (Jagacinski, Liao, & Fayyad, 1995; Vieluf et al., 2013). Thus, the result of the current study extended prior findings by demonstrating that tDCS could improve the spatial feature of rhythmically changing the force control ability. This protocol could thus also be used to improve performance deficits due to abnormal spatial force controls in an ageing population. Furthermore, we suggest

that when tDCS is used to improve motor learning of the spatial feature of rhythmically changing force control ability, the left M1 should be chosen as the target brain area; and when the purpose is to improve motor learning of the gradually decreasing force control ability, the left M1 and left DLPFC could be the target brain areas.

Since this explorative study sought to detect possible different learning effects of tDCS over different brain areas and under diverse task constraints, however as the young participants may exist ceiling effect during the learning process, and the insufficient sample size might have precluded confirmation of the hypothesized difference.

5. Conclusions

In the present study, the effect of tDCS over M1 and DLPFC on the learning of bimanual isometric force control was investigated in four different BFM tasks. We conclude that tDCS over the left M1 and DLPFC has a beneficial effect on the learning of bimanual force control.

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Disclosure of interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humov.2019.03.002.

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