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#### The Effect of Brain Hemisphere Stimulation and How to Specialize Motor Task Programming: A Transcranial Direct Current Stimulation Study

Mostafa TEYMURI KHERAVI<sup>1</sup>, Alireza SABERI KAKHKI<sup>1</sup>, Hamidreza TAHERI<sup>1</sup>, Ali GHANAEI CHAMANABAD<sup>2</sup>, Mohammad DARAINY<sup>3</sup>

<sup>1</sup>Ferdowsi University of Mashhad, physical education and sport science, Mashhad, Khorasan Razavi, Iran, Islamic Republic Of <sup>2</sup>Ferdowsi University of Mashhad, Psychology, Mashhad, Khorasan Razavi, Iran, Islamic Republic Of <sup>3</sup>McGill University, Psychology, Montreal, Quebec, Canada

#### Summary

**Background and Purpose:** Studies have unanimously supported that left-hemisphere specialization is greater than the right hemisphere for representation of learned actions and motor learning, but it is not clear as to whether there is a particular specialization related to motor programming. This study investigated the issue by comparing the effect of transcranial direct current stimulation (tDCS) of the primary motor cortex (M1) on the right and left hemispheres.

**Methods:** Participants (n=53) practiced special motor patterns for a period of three days and the left M1 and right M1 groups received simultaneous stimulation in the left and right M1, respectively. Data obtained from root mean square (RMS) error, movement time, RMS error/movement time ratio, and skill were analyzed using repeated measures ANOVA.

**Results:** The results showed that although all groups experienced a significant reduction in RMS error over time relative to the pretest stage (P <0 .05), the left M1 group had significantly lower RMS error only in the retention stage compared with the other groups (P <0. 05). Also, the results showed that the progress rate in skill factor was greater in the left M1 group than in the right M1 and control groups.

**Conclusions:** The left hemisphere is probably more specialized in motor programming, and this laterality is expected to be through the motion-consolidation mechanism.

**Key words:** Transcranial Direct Current Stimulation, Primary Motor Cortex, Motor programming, Hemispheric Specialization

#### Beyin Hemisfer Stimülasyonunun Etkisi ve Motor Beceri Programlamada Özelleşme: Bir Transkraniyel Direk Akım Stimülasyonu Çalışması

#### Özet

**Amaç**: Çalışmalarda sol hemisfer özelleşmesinin öğrenilmiş hareketlerin temsili ve motor öğrenme için sağ hemisfere göre daha büyük olduğu gösterilmiştir. Ancak motor programlamaya yönelik ayrı bir özelleşme olup olmadığı açık değildir. Bu çalışmada sağ ve sol hemisfer üzerindeki primer motor kortekse (M1) transkraniyel direk stimulasyonun (tDCS) etkisinin karşılaştırılması araştırılmıştır.

**Yöntem**: Katılımcılar (n= 53) üç gün periyodunda özel motor paternleri çalışmış, sol M1 ve sağ M1 grupları sırasıyla sol ve sağ M1'e eş zamanlı stimulasyon almıştır. Kök ortalamasının

karesi (RMS) hatası, hareket zamanı, RMS hatası/hareket zamanı oranı ve becerilerden elde edilen veriler tekrarlayan ANOVA ölçümleri ile analiz edilmiştir.

**Sonuçlar:** Sonuçlar tüm gruplarda zaman içerisinde test öncesi duruma göre RMS hatasında anlamlı düşüklük saptandığını (p<0.05), sol M1 grubunda retansiyon döneminde diğer gruplarla karşılaştırıldığında anlamlı olarak daha düşük RMS hatası elde edildiğini (p<0.05) göstermiştir. Ayrıca sonuçlar beceri faktoründe ilerleme oranının sol M1 grubunda sag M1 grubu ve kontrol grubuna gore daha büyük olduğunu göstermiştir.

**Sonuç:** Sol hemisfer motor programlamada olasılıkla daha özelleşmiştir ve bu lateralitenin motor-konsolidasyon mekanizmasI dolayısıyla olduğu düşünülmektedir.

Anahtar kelimeler: Transkraniyel direk akım stimülasyonu, primer motor korteks, motor programlama, hemisferik özelleşme

### INTRODUCTION

Transcranial direct current stimulation (tDCS) is a non-invasive and painless procedure that uses a direct electrical current to stimulate specific areas of the brain. There are two types of stimulation with tDCS: anodal stimulation to excite neuronal activity, and cathodal stimulation to inhibit or reduce neuronal activity (1). During anodal stimulation, the current depolarization of the resting causes membrane. and increased neuronal excitability allows for more spontaneous cell firing. In contrast, during cathodal stimulation, the current causes hyperpolarization of the resting membrane and thus reduced excitability and decreased spontaneous cell firing (2,3). Studies show enhance that tDCS can cognitive performance in many tasks, depending on the areas of the brain stimulated (1).

Concerning the effects of tDCS on motor tasks, the results of studies suggest that tDCS can result in motor cortex excitability and thereby accelerate and improve motor learning by facilitating the functioning of the area stimulated which can help to save neuron potential and improve motor performance and learning (1,4,5). The effect of tDCS is not limited to the excitation time because it leads to lasting effects in cortical excitability through structural and functional changes in cortical areas and thus facilitates functioning of the area stimulated (6).

Different areas of the brain are responsible for various functions, and each has a greater specialization in specific acts (7-9). Findings have demonstrated that tDCS could greatly improve performance in these areas (1,5,8,10).

Specialization of the nervous system can be monitored both inter- and intrahemispherically. The division of functions, and as a result, collaboration between the two hemispheres to execute a skill relative intra-hemispheric cooperation to and divisions leads to a reduction in workload and thus better control of skills (11). Evaluation of studies conducted on brain specialization indicates interesting points regarding the role of each hemisphere in the control of various aspects of motor skills. Stöckel and Weigelt showed that the left-hemisphere was specialized in controlling movement sequences and timing, movement trajectory, and dynamic aspects of tasks (7). Accordingly, it seems that the left hemisphere is more specialized in feed-forward and motor-programming processes than the right hemisphere. For example, Mutha et al. found that lefthemisphere damage, not right, led to incompatibility with deviations in the initial direction of motion, which is an important characteristic of motor programming (12). To support this, some researchers reported that the left hemisphere mainly used predictive for specific coordination mechanisms patterns, and left hemisphere damage

caused poor coordination among movement components (13-15). Other evidence related to higher left-hemisphere specialization in motor programming could be the greater apraxia observed after damage to the left-hemisphere than in the right hemisphere, as well as the important role of the left hemisphere in the recall and implementation of previously learned motor skills(16,17,18). It should be noted that studies on brain function suggest that the premotor cortex, especially M1 may be more important in the process of motor programming (19,20-24) .

Similar to the study of Schambra et al. on hemispheric specialization in motor skill learning using tDCS, the researchers in the present study examined the existence of hemispheric specialization in motor programming using tDCS because motor learning is associated with structural and changes in functional some neural networks such as the M1 and the beneficial effects of tDCS on motor learning is concerned with strengthening neural networks and improving the physiologicalchanges (1, 8, 25, 26).cellular Thus, stimulation in a specific area of the brain along with practice is predicted to cause improved performance of the relevant area. The aim of the present study was to investigate the effects of M1 stimulation in hemispheres the two and their specialization in motor programming.

## MATERIAL AND METHODS

Participants: Fifty-three volunteer male students aged  $21.34 \pm 1.61$  years took part in this study, which was approved by our Faculty of Physical Education and Sport Sciences (code: 3/41014). Participants completed an informal consent form to participate in the study. All experiments were performed in the Motor Behavior Laboratory of our faculty. Inclusion criteria were general health, right-(using Edinburgh handedness the Handedness Inventory), age range of 18 to

25 years, lack of upper extremity musculoskeletal disorders, no chronic neurologic, psychological or medical lesions, and non-use of psychotropic drugs (27).

**Groups:** The participants were randomly divided into four groups: right M1 (n=14), who practiced motor patterns along with right-hemisphere stimulation; left M1 (n=13), who practiced motor patterns with left-hemisphere stimulation; sham tDCS (n=11), who practiced motor patterns and received stimulation over 15 s at the beginning of the 20-min period; and the control group (n=15), who practiced motor patterns without any stimulation.

Task: To perform the task (Figure 2), purpose-designed software was installed on a computer; the validity of which was determined as 0.78 using the test-retest method. Then, a light pen graphics tablet (Genius Pensketch M912A, 12 x 9 inches) was used to perform the patterns on the screen. Three patterns were used to practice the program adapted from the method of Wulf and Schmidt (28). The appeared randomly to patterns the participants who executed them after observation. Each pattern was displayed for one second and then disappeared. The participants were asked to move the pointer to a start point on the left side of the monitor using the light pen (small red circle in Figure 2). This action turned the vellow point in the top-left corner of the monitor to green, indicating the accuracy of this action and readiness to draw the pattern. The time was recorded for participants immediately after they left the start point. The movement was completed by quickly passing from the end line, determined by a non-visible vertical line at the end of motion. During pattern drawing, the pointer trace (the route passed by the person) did not remain on the monitor prevented screen. This action the participant from using simultaneous feedback to draw patterns. Participants

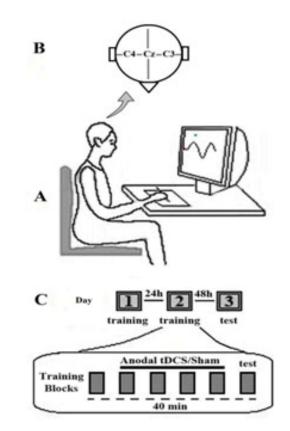
were asked to perform the observed pattern with speed and automatically in the range of 3.3 seconds. This practice approach encouraged participants to use feedforward visual information and predictive mechanisms for motor programming, and then performed the pattern. After drawing the pattern, the participants compared the drawn pattern with the criterion pattern. In this way, they identified their error rate to obtain proper feedback for movement correction in the next trial. Root-meansquare error (RMSE) is a frequently used measure of the differences between values predicted by a model or an estimator and the values actually observed (29). In motor behavior studies, RMS error is usually used to measure the accuracy of motion patterns performed (30,31). In this study, we used RMS error to measure the accuracy of motor programming bv comparing the patterns performed by participants with criterion patterns. The values of RMS error, movement time, RMS error/movement time ratio, and skill (Equation 1) were used to determine the levels of learning in motor programming. Because skill means faster and more accurate performance of tasks, and given the inverse relationship among RMS error and movement time with skill, the following equation calculated the progress percentage of participants in skill:

(Equation 1) Skill=1/RMS error×1/movement time×100

Stimulation: Two 25-cm2 electrodes soaked in a saline solution were used for stimulation using tDCS (Oasis Pro, Mind Alive). According to the Brodmann area and 10-20 systems, the anode was placed on C3 and the cathode on C4 during practice for left M1 stimulation, and their right reversed for order was M1 stimulation (32,33). The tDCS was used for each electrode during practice with 2mA voltage for 20 min, current density 0.08 mA/cm2 (34). Stimulation lasted for 15 s in the sham tDCS group (8,35). It is noteworthy that participants were not aware of the type of stimulation received. The participants were frequently asked about possible stimulation adverse effects (e.g., headache, skin irritations, inattention, and drowsiness) during all practice sessions (8).

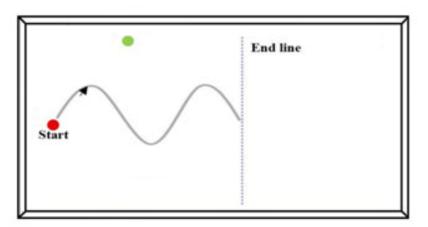
Practice paradigm: The practice paradigm was developed according to Schambra et al. and then approved by a pilot study (8). Next, the participants conducted a pretest stage (five-trails). The acquisition stage was conducted in a twoday period and participants practiced four blocks (30 trails) per day. The acquisition test was performed at the end of each day and the retention test two days after the last training session (Part c, Figure 1). Anodal tDCS stimulation during the last three blocks was given each dav for approximately 20 min. The participants were allowed to rest for 30 s between each two blocks.

**Psychological** assessments: A11 participants were asked for information including sleep duration, visualization ability, handedness, and perceptions of tDCS (Table 1) (8,27,36). In relation to their perception of stimulation, they described their feelings about the use of tDCS in the form of perception of stimulation. Statistical analysis: The values of RMS error, movement time, RMS error/movement time ratio, and skill in the four groups (left M1, right M1, sham tDCS, and practice) in four tests (pretest, acquisition 1, acquisition 2, retention) were analyzed using repeated measures ANOVA. The mean age of participants in each group, sleep duration, visualization ability, and handedness were also analyzed using one-way ANOVA. One-way ANOVA was also used to compare the groups at any of the stages and the Bonferroni post hoc test was used to determine significance between the pairstudied groups. Significance was assessed at the level of P < 0.05 in two tails.



**Figure 1:** Methods: A: an overview of research: Four groups performed the task using a light pen on a 12 x 9-inch screens. B: stimulation paradigm: The anode was on the C3 and the cathode on C4 during practice for the left M1 stimulation and their order was reversed for right M1 stimulation. C: practice paradigm: Over a three-day period, first the subjects participated in a pretest, and then practiced for two days. After 48 h, they took part in the retention tests. The participants practiced four, 30-trial blocks in each training session for approximately 40 min. Stimulation was applied for 20 min during the last three blocks. An acquisition test was performed after five min.





**Figure 2:** The Motor Task: The paradigms were displayed randomly to the participants. Then they put the pointer on the start point (red spot) with the light pen to perform the paradigm. At that time, the yellow spot in the top left of the screen changed to green, indicating readiness to perform the paradigm. The participants performed the paradigm with speed and accuracy and crossed the pointer quickly from the non-visible end line.

## RESULTS

The characteristics, including the number of participants, age, visualization ability, handedness, and sleep duration in each group are shown in Table 1.

**RMS error:** The mean pattern error of the four groups (left M1, right M1, sham tDCS, and practice) in the four tests (pretest, acquisition 1, acquisition 2, retention) are presented in Figure 4a. The results showed that the main effect of time was significant  $(f_{(3, 147)} = 21.571, P < .001,$  $\eta^2 = 0.306$ ) such that significant differences were observed between the pretest and all stages ( $P \leq .05$ ). However, the main effect of the group  $(f_{(3, 49)} = 1.676, P = .184, \eta^2 =$ 0.093) and interaction effect between time and group (f<sub>(9, 147)</sub> = 1.227, P = .283,  $\eta^2$  = 0.070) were not significant. One-way ANOVA was used to compare the groups at any of the stages. There were no significant differences between the groups  $(f_{(3)} = 0.351, P = .789)$  in the pretest, but significant differences were observed in the retention stage ( $f_{(3)} = 4.476$ , P = .007). The Bonferroni post hoc test only showed a difference between the left M1 and practice groups (P = .004) (Figure 3), thus the RMS error in left M1 was greatly decreased.

**Movement time:** The mean movement times of the four groups in the four tests are shown in Figure 4b. The main effect of time ( $f_{(3, 147)} = 1.092$ , P = .354,  $\eta^2 = 0.022$ ), group ( $f_{(3, 49)} = 0.346$ , P = .792,  $\eta^2 = 0.021$ ), and the interaction effect between time and group ( $f_{(9, 147)} = 0.112$ , P = .999,  $\eta^2 = 0.007$ ) were not significant. The results also showed no significant

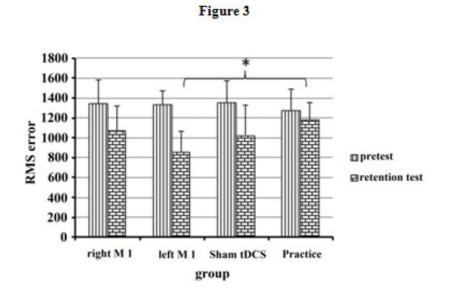
differences between the groups at any of the stages (P > .05).

**RMS error/movement time:** The RMSE error/movement time ratio was calculated, and the means obtained for the four groups in the four tests are presented in Figure 4c. The results revealed a significant effect of time ( $f_{(3, 147)} = 7.354$ , P < .001,  $\eta^2 = 0.130$ ); the Bonferroni test revealed a significant difference between the pretest and all stages ( $P \leq .05$ ). However, the main effect of group  $(f_{(3, 49)} = 0.648, P = .588, \eta^2 =$ 0.038) and the interaction effect between time and group  $(f_{(9, 147)} = 0.467, P = .895,$  $\eta^2 = 0.028$ ) were not significant. In addition. the results indicated no significant difference between the groups at any of the stages (P > .05).

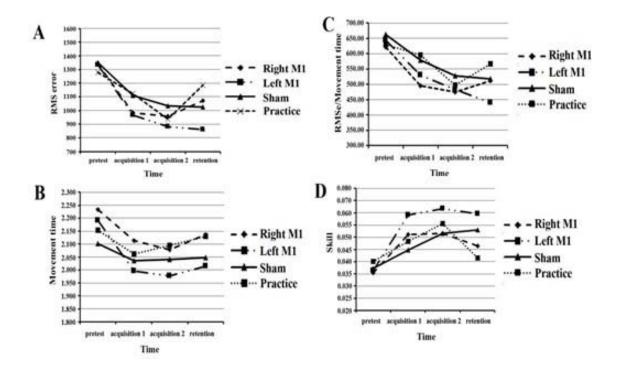
Skill: The mean scores of skill (equation 1) for the four groups in the four tests are shown in Figure 4d. The results showed that the main effect of time was significant  $(f_{(3, 147)} = 20.407, P < .001, \eta^2 = 0.294);$ there was a significant difference between pretest and all stages ( $P \le .05$ ). The results also proved a significant effect of group  $(f_{(3, 49)} = 2.719, P = .050, \eta^2 = 0.143).$ However, the interaction effect between time and group  $(f_{(9,147)} = 1.886, P = .058,$  $\eta^2 = 0.104$ ) was not significant. The results indicated a significant difference between the groups only in the retention stage ( $f_{(3)} =$ 5.757, P = .002). The Bonferroni post hoc test confirmed this difference between the left M1 and right M1 groups (P = .042), as well as between the left M1 and practice groups (P < .001) (Figure 5); the left M1 group had the greatest skill to perform the task.

	n <sup>a</sup>	Age (years) <sup>b</sup>	Imagery ability <sup>c</sup>	Handedness <sup>d</sup>	Sleep duration (h) <sup>e</sup>
Right M1	14	21.42±1.55	49.14±6.78	96.42±4.97	7.14±1.02
Left M1	13	$20.69 \pm 1.60$	46.30±6.93	95.38±6.60	7.61±1.12
Sham tDCS	11	$21.09 \pm 1.44$	44.63±7.71	96.34±6.74	7.27±1.10
Practice	15	22.00±1.69	45.26±6.38	94.66±6.39	7.06±1.09
P value*	-	0.18	0.354	0.856	0.571

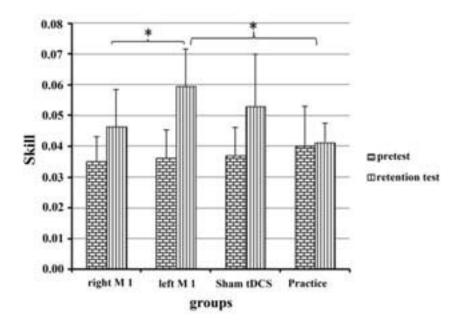
**a:** The number of participants in each group; **b:** Age (years); **c:** Visualization ability was assessed using the visualization ability inventory of Hall and Martin (1997) with eight questions (score 1 for the least ability and score 7 for the highest ability); **d:** Handedness was measured using the Edinburgh Handedness Test containing 10 questions with scores ranging from 0 to 100, **e:** Sleep duration per hour; **g:** Difference between groups in any variable



*Figure 3: RMS* error of the groups in two pretest and retention phases. \*: indicating significant difference for pretest between the two left M1 and practice groups



*Figure 4: a: RMS error of four groups in four tests, b: movement time of four groups in four tests, c: RMSE error/movement time ratio of the four groups in the four periods, d: progress in skill of four groups in the four tests.* 



*Figure 5:* Scores of skill among the groups in the pretest and retention phases. \*: There are significant differences between the left M1 and right M1 groups as well as between the left M1 and practice groups; the left M1 group shows the highest skill.

## DISCUSSION

The results obtained from the present study showed that anodal stimulation in the left M1 along with cathodal stimulation in the right M1 relative to reverse status led to lower RMS error in the retention stage compared with the practice group, which occurred 48 h after the last training session. However, it is likely that the reduction in RMS error is associated with increased movement time. The movement time was not significant between groups. Concerning the most important variable, the skill that involves the effect of both RMS error and movement time variables and means faster and more accurate performance of task, the results indicated that the left M1 group had greater skill compared with the right M1 group and practice group. This laterality was only observed retention in the stage. Interestingly, information on perception of stimulation demonstrated that nine subjects performed the patterns automatically and involuntarily (left M1: six, sham tDCS: two, and right M1: one). This emphasizes more automated implementation of learned patterns within left hemisphere stimulation. Therefore, reduced RMS error, increased skill (i.e., faster and more accurate perform of movement), and more automated implementation due to left hemisphere stimulation showed greater left hemisphere specialization in motor programming.

#### Investigation of tDCS and Specialization

During motor learning, several structural and functional changes occur in some neural networks such as the M1, and it has been suggested that the beneficial effects of tDCS on motor learning are related to strengthening these neural networks (1,25,26).The M1 stimulation and enhanced excitability could be due to increased stimulatory neurotransmitters or reduced inhibitory neurotransmitters in the M1increased level of brain-derived

neurotrophic factor (BDNF) and its positive impacts on encoding processes in motor memory in the M1, which has important effects on motor learning (9,32,37-39). The M1 is a key structure in neural networks involved in motor learning, which can help motor learning through stimulation (26,40). It has been predicted that the role of hemispheric specialization can be determined in motor programming using M1 stimulation in the two hemispheres, combined with practice, because of the positive effects of tDCS along with practice on motor learning. Schambra et al. Examined the role of hemispheric specialization in motor learning using transcranial direct current stimulation (8). The results of the present study also emphasize the possibility of leftspecialization hemisphere in motor programming using tDCS. However, it should be remembered that there was no significant difference between the groups in acquisition stages, and the significant difference between the groups of lefthemisphere tDCS and right-hemisphere tDCS was only observed in the retention stage. Therefore, it is anticipated that the effects of tDCS are further related to consolidation of motor programming in the left hemisphere. Reisa et al., Muellbacher et al., Nitsche et al., Reisa et al., and Robertson et al. also demonstrated the consolidation effects of tDCS during left M1 stimulation for motor learning (5,10,40,41) On the other hand, some research on the role of the M1 in motor learning indicated that M1 areas were important in motor skill consolidation (26,40,42,43). Therefore, we suggest that improved tDCS leads to motor programming through consolidation motor programs in the M1.

# How is the left hemisphere more specialized in motor programming?

Quantifying generalized patterns is a useful method to infer the existence of a neural

structure of the motor-learning process (motor programming) in the brain (44,45). The present study also examined the motor-programming process and hemispheric specialization by quantifying motion patterns and using the RMS error and movement time of the patterns. The same thing happens in the first part of the reaching movement because the first part of this movement (i.e. the part of increased acceleration) is associated with open-loop and control processes predictive mechanisms, as well as programming the best sequence of muscle activities before running the movement (46,47). Some evidence on patients with unihemispheric lesions suggests that the parietal lobe of the left hemisphere plays a key role in predictive and feed-forward mechanisms (13,48). For example, recent findings in patients with limb apraxia, usually occurring after left parietal damage, support the idea of left parietal mediation in predictive mechanisms and motor programming (3,16,49). Herefore, we the existence of speculated left specialization in hemispheric motor programming in healthy individuals. Our results showed that anodal stimulation in the left M1 leads to further improvement in motor programming. These results are consistent with a study conducted by Stöckel and Wang (50). Their results showed that direction of transmission between the two members could change depending on conditions. Laterality in the dynamic information transmission (power characteristic of motor impulse). as programming, from right to left can be indicative of left hemisphere specialization in feed-forward mechanisms and motor programming because each cerebral hemisphere controls the contralateral limbs, and there is more direct connection between the cerebral hemispheres and the contralateral member (51,52). In addition, Schambra et al proposed that if one hemisphere has more specialization for motor learning compared with the opposite hemisphere, its performance increased through stimulation would lead to better performance and learning than stimulation of the opposite hemisphere (8). It was suggested that the left hemisphere was probably more specialized in motor skill learning than the right one (8). Despite the fact that Schambra et al. did not report directly, it seems that their study task relied on feed-forward mechanisms and motor programming (8).

The results of Stöckel and Wang as well as Schambra et al. were consistent with the findings of the current study (8.50). However, our results are in contrast with the findings of Thomas et al. because they reported that there was no specific motor programming right for hand/left hemisphere vs. left hand/right hemisphere when performing a throwing shoulder task (53). It should be noted that Thomas et al examined healthy children as participants and used a motion-analysis device to investigate the existence of motor programming (53). Whereas according to Alexander et al the lateralization evidence can only be clearly seen after damage to the corpus callosum or to one hemisphere. Therefore, the reported conclusions cannot be controversial in terms of hemispheric specialization (52).

Totally based on previous reports and the results of this study, it can be suggested that the left hemisphere may have more specialization in feed-forward processes and motor programming. These findings can be interpreted using the Yadav and Sainburg hypothesis as a hybrid control of movement consisting of two parts (54). It states that each hemisphere is specialized for different motor-control mechanisms. A predictive control mechanism controls the trajectory of movement through motor programming using feed-forward information, and an impedance control mechanism is responsible for controlling final position accuracy of motion using sensory-motor feedback(54). In connection with the issue that specialization is poor (i.e., both hemispheres are involved in

processing but one more important) or strong (i.e., only one hemisphere is responsible for processing and the corpus callosum is necessary for functional integration) suggest that we this specialization is poor because practice and stimulation in the right hemisphere also improve motor programming (15). This is in line with the statement that each hemisphere is specialized for specific but complementary mechanisms (8,13,15).

## CONCLUSION

Considering the positive effects of electrical stimulation on motor learning and using this method to determine hemispheric specialization in motor learning, as well as improved motor programming by stimulating the M1 of the left hemisphere, it can be concluded that the M1 of the left hemisphere has more specialization than the right hemisphere in improving motor programming. This is consistent with Yadav and Sainburg's hypothesis, which proposed that lefthemisphere specialization controlled feedforward mechanisms, as well as with the Sainburg dynamic-dominance hypothesis emphasized left-hemisphere that specialization in open-loop control processes (54, 55).

#### **Future Research**

First, because the participants in the present study were all right-handed and all previous reports are on right-handed participants, the accuracy of specialization in left-handed persons merits further research. Second, due to the positive effects of tDCS stimulation on motor learning consolidation,(10,40,41) as well as the impact of electrical stimulation in the offline period, i.e., resting between sessions,(41) there is a need to develop and examine hypotheses regarding the consolidation impact of practice in training and resting periods. Third, given that motor learning has two components motor programming including and parameterization, (56) it is necessary to investigate the mechanisms of hemispheric

specialization in motor parameterization in addition to examining hemispheric specialization in motor programming using tDCS.

#### **Correspondence to:**

Alireza Saberi Kakhki E-mail: Askakhki@um.ac.ir

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