Research Article

The effects of transcranial static magnetic fields stimulation over the supplementary motor area on anticipatory postural adjustments

Daisuke Tsuru[a], Tatsunori Watanabe[a,1], Xiaoxiao Chen[a], Nami Kubo[a], Toru Sunagawa[a], Tatsuya Mima[b], Hikari Kirimoto[a, *]

[a] Department of Sensorimotor Neuroscience, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan
[b] Department of Analysis and Control of Upper Extremity Function, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan
[c] Graduate School of Core Ethics and Frontier Sciences, Ritsumeikan University, Kyoto, Japan

[1] Equal contribution to this study

*Corresponding author: Hikari Kirimoto, Ph. D.
Department of Sensorimotor Neuroscience, Graduate School of Biomedical and Health Sciences, Hiroshima University
734-8553, 1-2-3 Kasumi, Minami-ku, Hiroshima, Japan
Tel: +81-82-257-5445
E-mail: hkirimoto@hiroshima-u.ac.jp

Abstract

We investigated the influence of transcranial static magnetic field stimulation (tSMS) over the supplementary motor area (SMA) on anticipatory postural adjustments (APAs), in which the activation of the postural muscles of the legs and trunk that control standing posture precedes the activation of the prime mover muscles during rapid shoulder flexion movement. Eighteen subjects performed a self-paced rapid shoulder flexion task before, during, and after tSMS. Electromyogram (EMG) activity was recorded from the deltoid anterior (AD) as the prime mover muscle and the biceps femoris (BF) as the postural muscle during the task. The EMG latency difference (ΔEMG onset) between the two muscles was calculated by subtracting the EMG burst onset of the BF from that of the AD. The ΔEMG onset was significantly shortened, but center-of-pressure parameters were not affected after tSMS stimulation. These findings suggest that tSMS applied over the SMA could inhibitively modulate APAs function.

Keywords

Transcranial static magnetic stimulation

Non-invasive brain stimulation

Supplementary motor area

Anticipatory postural adjustments

Highlights

- Transcranial static magnetic field stimulation (tSMS) can reduce cortical activity
- The effect of tSMS over the SMA on APAs was investigated
- After 20 min of tSMS, the APAs function was impaired

Abbreviations: tSMS, transcranial static magnetic field stimulation; SMA, supplementary motor area; NIBS, non-invasive brain stimulation; M1, primary motor cortex; APAs, anticipatory postural adjustments; EMG, electromyography; AD, deltoid anterior muscle; BF, biceps femoris muscle

1. Introduction

Transcranial static magnetic field stimulation (tSMS) has recently been added to the family of inhibitory non-invasive brain stimulation (NIBS) techniques, such as low-frequency repetitive transcranial magnetic stimulation (rTMS) [1], continuous theta-burst stimulation (cTBS) [2], and cathodal transcranial direct current stimulation (tDCS) [3]. Oliviero et al. [4] first reported that the excitability of the primary motor cortex (M1) in the human brain can be reduced by application of static magnetic fields (SMFs) on the scalp with a strong cylindrical neodymium, iron and boron (NdFeB) magnet. Since then, this novel NIBS technique has become an increasingly useful tool to examine cortical function in healthy subjects. It has been demonstrated that tSMS applied over the M1 induces a reduction of cortical excitability, as measured by motor-evoked potentials [4-9], somatosensory-evoked potentials (SEPs) [10, 11], and intra-epidermal electrical stimulation-evoked potentials [12], and could also modulate motor learning [13, 14] and motor performance accuracy [15]. Furthermore, when SMFs were applied over the visual [16, 17] or temporal cortex [18], the function of visual and auditory systems was impaired. In addition, when applied over the visual [16] or the somatosensory cortex (S1) [19], electroencephalographic (EEG) α-oscillations were locally increased. In a more recent study, tSMS over the supplementary motor area (SMA) has been reported, at a behavioral level, to increase the time to initiate movement while decreasing errors in choice reaction-time tasks, and at the cortical level, to modulate the SMA resting-state functional magnetic resonance imaging (fMRI) activity and bilateral functional connectivity between the SMA and both the paracentral lobule and the lateral frontotemporal cortex [20]. Collectively, these results indicate the potential clinical application of tSMS for suppressing excessive activity of the SMA. Especially patients who have such neurological disorders as Parkinson's disease and Gilles de la Tourette syndrome may benefit from this new NIBS technique, as shown in previous rTMS studies [21-23]. As people with Parkinson's disease experience impaired motor planning and medication is not always effective, a recent meta-analytic review suggests that the development of rehabilitation techniques using NIBS tools may relieve this disorder [24]. Hence, the effects of tSMS over the SMA on motor planning, which is one of the key functions of the SMA, need to be clarified in detail.

Anticipatory postural adjustments (APAs) are a well-known representative function of the SMA and can be observed in various postural [25, 26], stepping [27-30], and bimanual load-lifting tasks [31]. In the first report to describe APAs [25], it was found that activation of the postural muscles of the legs and trunk that control standing posture preceded the activation of muscles directly involved in rapid upward arm movements. APAs function is markedly reduced in patients with Parkinson's disease [30]; as such, the basal ganglia–subthalamic nucleus–SMA loop is thought to be involved in APAs generation. Additionally, brain functional imaging studies combining fMRI or magnetoencephalography and EEG have shown increased excitability in the SMA, globus pallidus, putamen, and thalamus during bimanual load-lifting tasks [31]. Taking these studies into account, we have recently demonstrated that anodal tDCS over the SMA enhanced the APAs function in older adults [26], while cathodal tDCS acted inhibitively in young adults [32]. If the APAs function is affected by tSMS applied over the SMA, the tSMS would become a useful tool to modulate the excitability of not only the sensorimotor, visual, and auditory cortices, but also the SMA.

Consequently, this study aimed to investigate the possibility of novel, economical, convenient, and non-invasive modulation of APAs function by the application of tSMS over the SMA in healthy humans.

2. Methods

2.1.Subjects

Eighteen healthy subjects (11 males and 7 females, 21–32 years old) participated in this study. None were undergoing medical treatment for any condition. All participants were right-handed, as determined by Oldfield inventory scores of 0.9–1.0 [33]. Written informed consent was obtained from all participants before beginning the experiment, which was conducted according to principles of the Declaration of Helsinki. The experimental protocol was also approved by the Ethical Committee for Clinical Research of Hiroshima University (No. C20180015).

2.2 Experimental procedure

All subjects received tSMS or sham stimulation for 20 min at rest, followed by additional 3-5 min during a postural task in a counter-balanced order. To avoid carryover effects, each subject completed two sessions each on separate days. The subjects performed self-paced (every 20-30 seconds) rapid upward arm movements 10 times on a force plate before, during (immediately and 20 min after the start of stimulation), and after (immediately after and 10 min after) tSMS (Fig. 1a). They were required to move the dominant (right) arm upward and forward to 90 degrees of shoulder flexion at full speed and hold this position for 3 s. To maintain a constant center of pressure (COP), they were instructed to look at their own COP position shown on a monitor placed 1.5 m in front of them, and to try to maintain their COP position. During the task, electromyography (EMG) activity was recorded from the deltoid anterior (AD) as the prime mover muscle, and the biceps femoris (BF) as a postural muscle, according to previous APAs studies [25, 34, 35]. Additionally, an accelerometer was placed on the right wrist to evaluate movement of the arm. The use of two investigators allowed a double-blind study as follows: Investigator 1 selected and placed the real magnet or sham stainless cylinder; and Investigator 2, who was blinded to the type of intervention, recorded and analyzed the EMG and COP data.

2.3. tSMS

For tSMS, we used a cylindrical neodymium magnet (NdFeB; diameter, 50 mm; height, 30 mm) with a surface magnetic flux density of 534 mT, a maximum energy density of 49 MGOe, and a strength of 862 N (88 kgf) nominal value (NeoMag, Ichikawa, Japan). For sham stimulation, we utilized a non-magnetic stainless-steel cylinder of the same size and weight. The NdFeB magnet or the non-magnetic stainless-steel cylinder was settled on the scalp using a customized head gear (Fig. 1a). To stimulate the SMA, the NdFeB magnet or non-magnetic stainless-steel cylinder was placed 2 cm anterior to the Cz area of the international 10–20 system [26, 36].

2.4 COP recording

The subjects stood upright on the force plate (CFP400PA102RS, Leptrino, Japan) with equal weight on each foot. On the force plate, the outside of both fifth proximal phalanges was adjusted to the distance of shoulder peaks. The signals from the ground reaction were recorded at 200 Hz, low-pass filtered (20 Hz), and stored on a personal computer for off-line analysis (BSMLGR, Leptrino, Japan).

2.5 EMG and acceleration recording

The EMG signals of the right AD and BF muscles were recorded with surface bipolar electrodes (FSE-DEMG1, 4Assist, Japan). They were amplified (×100) and band-pass filtered at 20–450 Hz with an EMG amplifier system (FA-DL-140, 4Assist), and digitized at 2 kHz (PowerLab, AD Instruments, Australia). The acceleration of rapid arm movements was also recorded from 3-axis acceleration sensors (FA-DL-110, 4Assist) taped to the dorsal surface of the right wrist and stored on a personal computer for off-line analysis (LabChart v8.1.13, AD Instruments).

2.6. Data and statistical analysis

The baseline EMG activity for each muscle was determined by averaging the EMG data over a period of 100 ms prior to beginning any movement. The onset of EMG activity was defined as the point at which the EMG signal reached at least two standard deviations (SD) above the mean baseline for a period of at least 20 ms (Fig. 1b) [37, 38]. APAs function was evaluated by calculating the temporal difference between activation onsets of the AD and BF muscles (ΔEMG onset) [39]. The arm movement onset was defined as the point at which the acceleration signal reached at least three SD above the mean baseline (a period of 1000 ms prior to beginning any movement) for a period of at least 20 ms. The maximum acceleration and COP parameters were computed from the duration of arm movement. We calculated the maximum acceleration on y and z axes. Additionally, root mean square (RMS) area, sway path length, medio-lateral (ML) mean and max velocity, and antero-posterior (AP) average and max velocity were calculated from the COP data. For each parameter (ΔEMG onset, maximum acceleration, RMS area, sway path length, ML mean and max velocity, and AP average and max velocity) the average of 10 arm flexion movements was used for the following statistical analysis. We examined the effects of stimulation condition (tSMS and sham) and time (pre, during 0, during 20, post 0, and post 10) using a two-way repeated-measures analysis of variance (ANOVA). Significant differences were further analyzed with Bonferroni post hoc tests. All analyses were performed with IBM SPSS Statistics software version 21 (SPSS; IBM, United States), and the significance level was set at 5%.

3. *Results*

3.1 EMG activity after tSMS over the SMA

Figure 2a–c shows representative EMG waveforms recorded from the BF muscle during the self-paced rapid shoulder flexion task before, 20 min after tSMS started, and 10 min after tSMS removal.

Figure 3 shows the mean ΔEMG onset at different time points. The ΔEMG onsets before the stimulation were similar between conditions (sham: 96.2±10.8 ms, tSMS: 104.4±10.1 ms). A two-way repeated measures ANOVA on the ΔEMG onset revealed a significant main effect of time ($F_{(4,68)} = 4.063$, $p = 0.005$, $\eta^2 = 0.193$), and of stimulation condition × time interaction ($F_{(4,68)} = 4.251$, $p = 0.004$, $\eta^2 = 0.2$). There was no main effect of stimulation condition ($F_{(1,17)} = 0.839$, $p = 0.372$, $\eta^2 = 0.047$). A post hoc analysis revealed significant differences between before (pre) and 20 min after the stimulation started (during 20) ($p = 0.002$), and between immediately after (during 0) and 20 min after the stimulation started (during 20) ($p = 0.008$).

3.2. Upward arm movement acceleration

There was no significant main effect or interaction for the upward arm movement acceleration.

3.3 COP sway after tSMS over the SMA

There was no significant main effect or interaction for any COP parameter.

4. Discussion

The present study investigated the effect of tSMS applied over the SMA on the APAs function and found that ΔEMG onset between the AD and BF muscles during the rapid upward arm movement task was shortened after the stimulation in healthy subjects, although there was no change in the COP sway parameters. These findings suggest that tSMS over the SMA can decrease the timing of postural regulator muscle activity preceding rapid upward arm movements.

It has been reported that APAs are influenced by the COP position before the start of motion [39] and also by the arm movement acceleration in the upward arm movement task [40]. When the arm movements are slow with the body's center of gravity being positioned backward, forward movement of the body can be small, consequently shortening ΔEMG onset between the prime mover and postural muscles. In the present study, the subjects performed the rapid upward arm movements while maintaining a constant COP with visual feedback, and the maximum acceleration of arm movement did not differ between different time points (before, during, and after tSMS). Furthermore, although the weight of the magnet (or sham cylinder) could have influenced the APAs function and/or the arm movements, there were no significant differences in the ΔEMG onset between before and immediately after the stimulation started. Therefore, the changes in the ΔEMG onset during the stimulation can be attributed to tSMS over the SMA rather than confounding factors such as changes in COP position, decreased acceleration of upward arm movements over time, or the weight of the magnet on the head. It appears that similar to a previous study demonstrating increased reaction time and decreased error response in choice reaction task [20], tSMS influenced the SMA.

The mechanisms of tSMS are not completely clear. At the cellular level, SMFs with moderate intensity (1-1000 mT) magnetically reorient membrane phospholipids and ion channels via diamagnetic anisotropy [41]. The SMFs further inhibit voltage-gated calcium channel function and intracellular calcium flow, induce membrane depolarization, and decrease firing frequency [41-45]. In a previous study [11], we reported that tSMS over the M1 reduced the amplitude of the N33 component of SEP at C3' of the international 10–20 system of electrode placement, while tSMS over the SMA did not affect any SEP components of C3' or F3. We speculated that the SMA is likely to be a more difficult area to target with tSMS than the M1, since it is located in the interhemispheric fissure, where the magnetic field strength of tSMS may be attenuated to a non-effective level. However, given that the SMA can only be affected prior to exercise preparation, it might be inappropriate to verify the effect of tSMS over the SMA with changes in SEP amplitude at a resting condition. According to Coulomb's law, the magnetic flux density on the magnet surface decays in inverse proportion to the square of the distance. Based on actual measurements [11, 46] and computer simulations [47, 48], a sufficient static magnetic field can be considered to reach the cortex (an estimated distance of 2–3 cm from the scalp) to change excitability. Therefore, it does appear that tSMS can modulate the SMA, as shown in this and previous studies [20] through the diamagnetic anisotropy [41]. In addition to the excitability of the SMA, we hypothesize that tSMS over the SMA can modulate other brain regions within the APAs processing network, consistent with implications of other NIBS studies. In our previous study, we reported stimulation effects of simultaneous tDCS over the SMA and dorsal premotor cortex on distant sites, including M1 and S1 [49]. Accordingly, it is possible that the modulation of areas other than the SMA responsible for generating and outputting APAs (e.g., M1) in part accounted for the observed changes in the ΔEMG onset. Indeed, Pineda-Pardo and colleagues showed that tSMS over the SMA can induce the functional modulation of both the local cortical circuits below the magnet and distant functionally connected cortical networks [20]. Although the present study showed that the APAs function was modulated by the application of tSMS over the SMA, thus indicating the possible use of tSMS for suppressing excessive activity of the SMA and its networks, further studies are needed to elucidate the neurophysiological effects of tSMS over the SMA for clinical applications.

Since the postural muscles activate before the prime mover muscles to counteract expected postural perturbation ("motor synergies") [50] and thus to reduce body sway during rapid upward arm movement, the COP parameters were expected to be impaired (e.g., longer COP length and higher COP velocity) along with the shortening of ΔEMG after tSMS. However, in this study of younger adults, the COP parameters did not change after tSMS, despite the shortening of ΔEMG onset from 104 ms to 80 ms. In a previous study, we have reported that cathodal tDCS over the SMA of young adults decreased ΔEMG onset in the similar range and had no effect on COP parameters [32]. On the other hand, we have shown, in another study, that anodal tDCS over the SMA of older adults extended ΔEMG onset and decreased COP sway path length [26]. One possible explanation for these findings is that a relationship between length of ΔEMG onset and COP parameter is not linear but sigmoidal (Fig. 4). The lengthening of ΔEMG onset may improve COP parameters in individuals with initially reduced postural control (e.g., older adults), while COP parameters may stay at the highest level with slight shortening of ΔEMG onset in individuals with initially normal postural control (e.g., young adults). It can be inferred that the ΔEMG onset stayed within a range that did not affect the physical range of the COP parameters in young subjects. Indeed, no significant differences in posture stability have been reported with improved APAs function during development from children to adolescents [51]. Nevertheless, the exact mechanism should be explored in future studies.

6. *Conclusion*

Application of tSMS over the SMA shortens the ΔEMG onset between the prime mover and postural muscles in an upward arm movement task and thus alters the postural adjustment function of the SMA.

Disclosure

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

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Figure legends

Figure 1. Experimental procedure

Subjects performed self-paced rapid upward arm movements 10 times on a force plate pre, during 0, during 20, immediately after, and 10 min after tSMS. The NdFeB magnet or the non-magnetic stainless-steel cylinder was settled on the scalp using customized head gear (a). The onset of muscle activity was defined as the point at which the EMG activity reached at least two standard deviations above the mean baseline for at least 20 msec (b).

Figure 2. Electromyography (EMG) waveforms in the biceps femoris (BF) during a self-paced rapid shoulder flexion task for a representative case

Data from pre (a), during 20 (b), and post 10 (c) are presented. Latency differences (ΔEMG onset) were calculated by subtracting the time of EMG burst onset of the BF (BF onset) from that of the deltoid anterior muscle (AD) (AD onset).

Figure 3. Serial changes in average ΔEMG onset

Average ΔEMG onsets before (pre), during (during 0 and during 20 min), and after (post 10 and post 20 min) tSMS or sham procedures over the SMA are presented. Post-hoc analysis showed a significant difference between pre and during 20 min, and between during 0 and during 20 min (mean ± standard error of the mean). ($^{*}p < 0.05$).

Figure 4. Conceptual scheme of a relationship between length of ΔEMG onset and COP parameter

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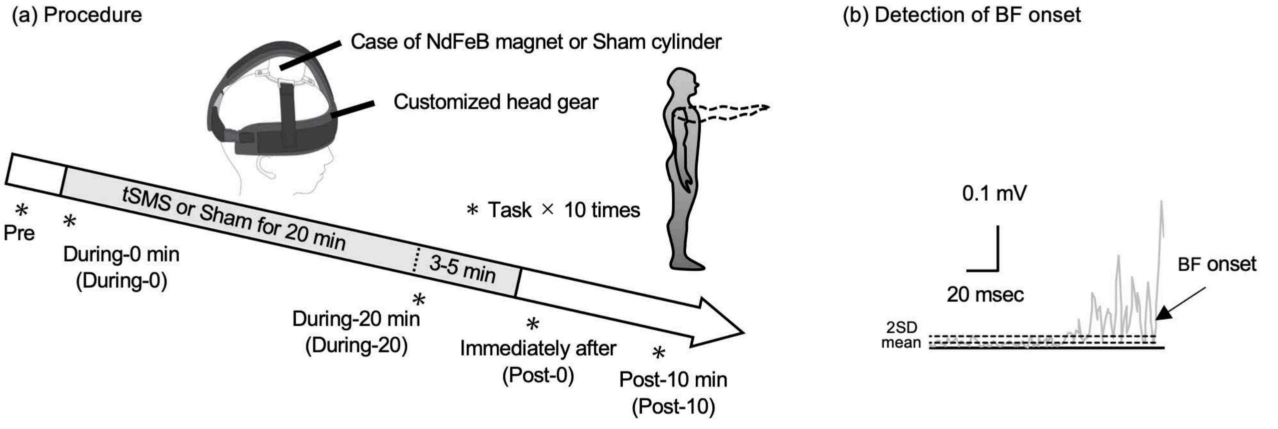
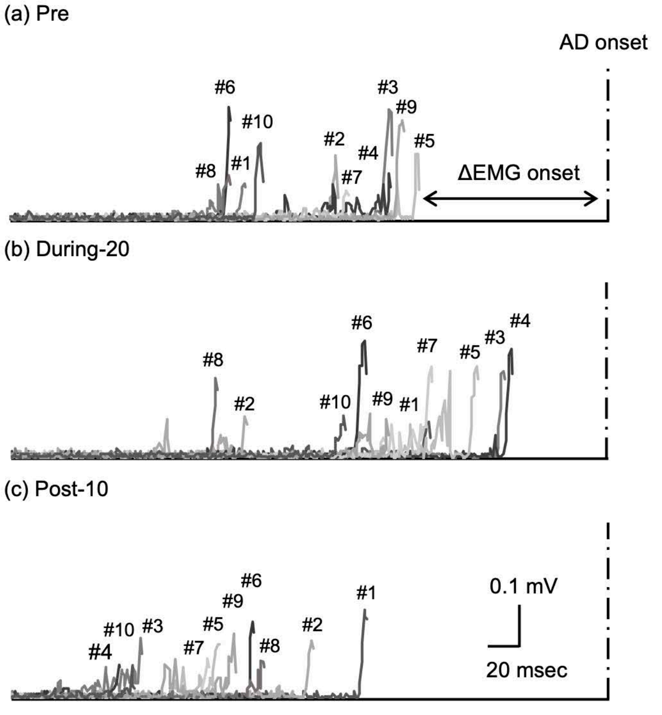

(a) Procedure
Case of NdFeB magnet or Sham cylinder
Customized head gear
tSMS or Sham for 20 min
3-5 min
* Task × 10 times
Pre
During-0 min
(During-0)
During-20 min
(During-20)
Immediately after
(Post-0)
Post-10 min
(Post-10)
(b) Detection of BF onset
0.1 mV
20 msec
BF onset
2SD
mean


(a) Pre
AD onset
#6
#10
#3
#9
#2
#4
#5
#8
#1
#7
ΔEMG onset
(b) During-20
#6
#4
#3
#7
#5
#8
#2
#10
#9
#1
(c) Post-10
#6
#9
#1
0.1 mV
#10
#3
#5
#2
#4
#7
#8
20 msec

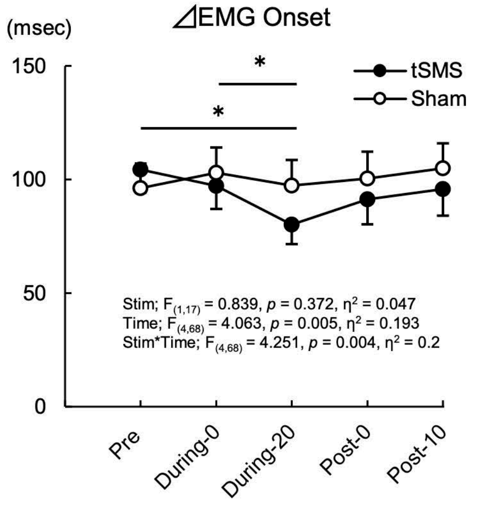
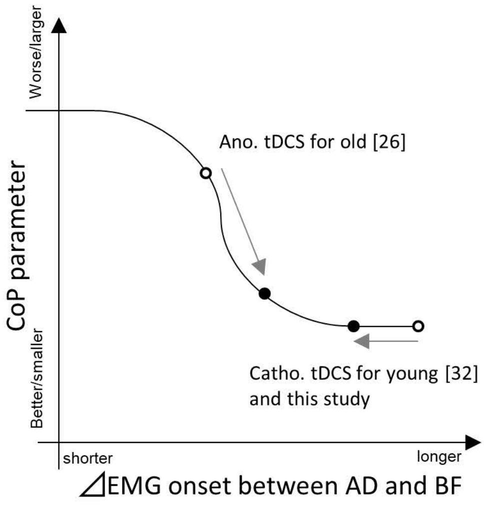

⊿EMG Onset
(msec)
150
100
50
0
*
*
tSMS
Sham
Stim; $F_{(1,17)}$ = 0.839, p = 0.372, η^2 = 0.047
Time; $F_{(4,68)}$ = 4.063, p = 0.005, η^2 = 0.193
Stim*Time; $F_{(4,68)}$ = 4.251, p = 0.004, η^2 = 0.2
Pre
During-0
During-20
Post-0
Post-10

Fig. 4



Worse/larger
CoP parameter
Better/smaller
Ano. tDCS for old [26]
Catho. tDCS for young [32]
and this study
shorter
longer
⊿EMG onset between AD and BF