Original article

Effects of continuous and intermittent voluntary movement tasks on the excitability of the corticospinal pathway

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Abstract

The corticospinal excitability changes transiently after brief finger movement task. Many previous studies have examined the effects of particular elements of a movement task on the change of corticospinal excitability; however, it has not been determined whether the change of corticospinal excitability is affected by the movement pattern. The present study aimed to determine whether the corticospinal excitability depends on movement patterns. A sample of 15 healthy adults repeatedly performed right index finger abduction at a frequency of 1 Hz and 10% of their maximum voluntary contraction under three movement conditions as follows: continuously for 10 minutes (Continue-10 min); continuously for 4 minutes (Continue-4 min), and intermittently (4 seconds of movement and 6 seconds of rest) for 10 minutes (Intermittent-10 min). Excitability of the corticospinal pathway was assessed before and after the movement task by transcranial magnetic stimulation. Results indicated that motor evoked potential (MEP) immediately decreased after the movement task in the Continue-10 min and Continue-4 min conditions but did not change in the Intermittent-10 min condition. The present study demonstrated that corticospinal excitability decreases following repetitive movement but not intermittent movement.

Introduction

Excitability of the corticospinal pathway is altered by voluntary movement [1-4]. The phenomenon whereby such excitability transiently increases after voluntary movement is called post-exercise facilitation (PEF) [3, 5-7]. A previous study demonstrated that PEF occurs after isometric wrist extension at 10%-50% of the maximum voluntary contraction (MVC) for 30 seconds [3]; furthermore, excitability of the corticospinal

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pathway increased by at least 2-fold immediately after wrist extension at 20% of the MVC for 10 seconds [3]. In another study, PEF occurred after isometric abduction-adduction of the index finger at 1 Hz for 60 seconds [5]. By contrast, the phenomenon wherein the excitability of the corticospinal pathway decreases after voluntary movement is called post-exercise depression (PED) [1, 2, 8-10]. PED was observed following isometric contraction performed at 50% of the MVC for 30 seconds until fatigue occurred [3]. In addition, PED occurred for 2 minutes following repetitive voluntary movement without fatigue (0.5 Hz, 10% MVC for 10 minutes) [11]. Although indices of spinal cord (F and H waves) and α-motor neuron and muscle (M wave) excitability do not change during PED [1, 3, 12, 13], short-interval intracortical inhibition (SICI) of the intracortical inhibitory circuit increases [10, 14]. This suggests that the mechanism underlying PED involves changes in intercortical interneuron excitability. However, the elements of a movement task that cause PED and PEF have not yet been identified.

Previous studies found that excitability of the primary motor cortex changed following an intervention using peripheral electrical stimulation (PES) [15-20]. Intermittent PES (4 seconds of stimulation and 6 seconds of rest at 30 Hz with intensity set as the exercise threshold) increased the excitability of the corticospinal pathway [16, 21]. Andrews et al. [15] reported such an increase following intermittent PES at 30 Hz for 20 minutes (4 seconds of stimulation and 6 seconds of rest with intensity set as the motor threshold). By contrast, continuous PES (for which intensity is set at the sensory threshold) decreased excitability of the corticospinal pathway [20, 22]. Furthermore, previous studies using repetitive transcranial magnetic stimulation found decreased and increased excitability of the corticospinal pathway after continuous and intermittent theta burst stimulation (TBS), respectively [23]. On the basis of these reports, interventions that produce intermittent stimulation may be involved in increased excitability of the corticospinal pathway. However, it is unclear how corticospinal excitability is affected by intermittent voluntary movement. Therefore, the purpose of this study was to examine the changes in corticospinal excitability after intermittent and continuous voluntary movements. We hypothesized that intermittent voluntary movement would increase corticospinal excitability, as would PES and TBS, whereas continuous voluntary movement would decrease corticospinal excitability, consistent with the findings reported in previous studies. If intermittent voluntary movements cause an increase in the corticospinal excitability, it will lead to improved motor performance in patients with stroke.

Materials and Methods

1. Participants

A sample of 15 healthy subjects who were right-handed (5 females; mean age ± standard deviation, 22.8 ± 1.3 years) participated in this study. All participants were provided a sufficient verbal and written explanation of the study, then signed and placed their seals on a consent form. The present study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Niigata University of Health and Welfare (Approval No:18186-190613).

2. Measurements

1) Electromyogram (EMG) measurement

EMG measurement targeted the right first dorsal interosseous (FDI) muscle, which was monitored with disposable Ag/AgCl electrodes in a belly-tendon montage. The earth electrode was wrapped around the right forearm. The EMG signals were amplified by an amplifier (A-DL-720-140, 4 Assist, Tokyo, Japan), processed by an A/D converter (Power Lab, AD Instruments, Colorado, USA) at a sampling frequency of 4 kHz, and then stored on a computer. For EMG analysis, 20 Hz high-pass filter was employed along with biologi-

cal signal analysis software (Lab Chart 7, AD Instruments, Sydney, Australia).

2) Motor evoked potential (MEP) measurement

Transcranial magnetic stimulation (TMS) was delivered through a figure-8 coil (9.5 cm diameter) that was connected to a Magstim 200 stimulator (Magstim, Dyfed, UK). The coil was held tangentially to the skull over the left primary motor cortex (M1) with the handle pointing posterolaterally at 45° to the sagittal plane in the position producing the largest MEPs from the right FDI muscle. The position and orientation of the coil were marked by magnetic resonance imaging (MRI) using the Visor2 TMS neuronavigation system (eemagine Medical Imaging Solutions GmbH, Berlin, Germany), and held in place. T1-weighted images were obtained using a 1.5 T MRI scanner (SIGNA HD, GE Healthcare, Milwaukee, WI, USA) before initiating the experiment. The TMS intensity was set to evoke an MEP of approximately 1 mV in the right FDI muscle. Consistent with previous studies [20, 24-26], TMS was delivered at a rate of 0.2 Hz during data collection, which was performed 15 times at rest [26].

3. Movement task

During the experiments, participants were seated in a comfortable position with their right upper extremity placed on an armrest and their wrist in a pronated position. The movement task was conducted with the right hand placed on the voluntary movement device (Figure 1). The subjects performed repetitive abduction movements of the right index finger. The movement intensity was set

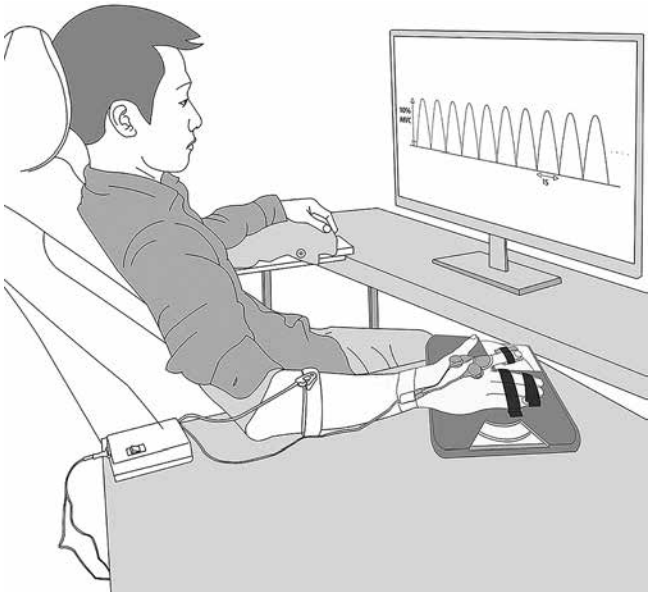

Figure 1. Illustration of the position of the participant while performing the movement task.
The participant was seated in a chair with correct posture and right hand placed on a table, and instructed to perform the movement tasks while looking at the monitor. Abduction of the right index finger at 10% of the maximum voluntary contraction (MVC) and a frequency of 1 Hz was performed under three movement task conditions as follows: continuously for 10 minutes, continuously for 4 minutes, and intermittently (4 seconds of movement and 6 seconds of rest) for 10 minutes. The participant adjusted the contraction intensity to coincide with 10% of his or her MVC in all three conditions.

at 10% of the MVC, which the participant achieved by tracking the rectified and smoothed EMG data on a display while performing the movement task. Abduction of the right index finger was performed at 1 Hz in three movement conditions (Figure 2) as follows: continuously for 10 minutes (a total of 600 repetitions; Continuous-10 min); continuously for 4 minutes (a total of 240 repetitions; Continuous-4 min); and intermittently for 10 minutes (4 seconds of movement and 6 seconds of rest for a total of 240 repetitions; Intermittent-10 min) [16]. Each participant performed each condition in a random order with a rest period of at least 3 days between experiments.

4. Experimental protocol

The experimental protocol (Figure 3) began with measurement of the MVC followed by a 30-second movement trial. The baseline MEP was recorded (Pre), and the movement task in the designated condition was performed. MEP was recorded immediately (Post0), 5 minutes (Post5), 10 minutes (Post10), 15 minutes (Post15), and 20 minutes (Post20) after the movement task.

5. Data analysis

A mean peak-to-peak value was calculated for 13 MEP waveforms after subtracting 2 waveforms with the maximum and minimum amplitudes from 15 waveforms that were recorded at each time point. Two-way repeated-measures ANOVAs with TASK factors (Continuous-10 min, Continuous-4 min, and Intermittent-10 min) and TIME factors (Pre, Post0, Post5, Post10, Post15, and Post20) were used to compare MEP amplitudes before and after the movement task conditions. Tukey HSD

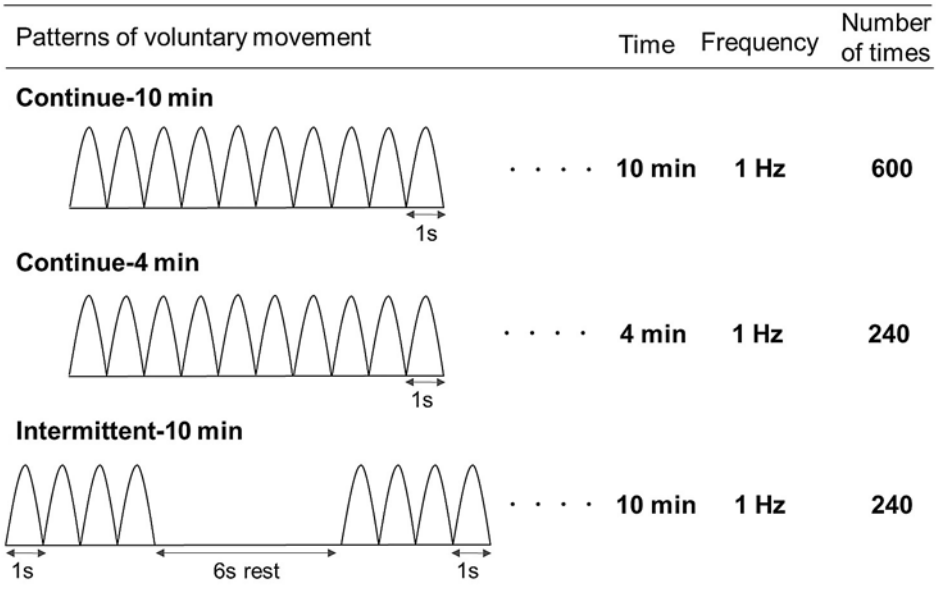

Figure 2. The three voluntary movement task conditions.
Abduction of the right index finger at 10% of the maximum voluntary contraction and a frequency of 1 Hz was performed under three movement task conditions as follows: continuously for 10 minutes (a total of 600 repetitions; Continuous-10 min); continuously for 4 minutes (a total of 240 repetitions; Continuous-4 min); and intermittently for 10 minutes (4 seconds of movement and 6 seconds of rest for a total of 240 repetitions; Intermittent-10 min).

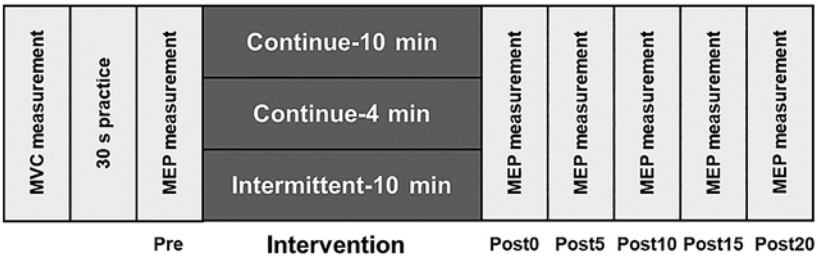

Figure 3. Experiment protocol.
After recording the maximum voluntary contraction (MVC) and determining movement intensity, an exercise trial was performed for 30 seconds (s). The motor evoked potential (MEP) of 15 waveforms was recorded at baseline (Pre); then, the movement task was performed by the participant (Intervention). The MEP of 15 waveforms was recorded immediately (Post0), 5 minutes (Post5), 10 minutes (Post10), 15 minutes (Post15), and 20 minutes (Post20) after the task. Continuous-10 min, abduction of the right index finger performed continuously for 10 minutes; Continuous-4 min, abduction of the right index finger performed continuously for 4 minutes; Intermittent-10 min, abduction of the right index finger performed intermittently (4 seconds of movement and 6 seconds of rest) for 10 minutes.

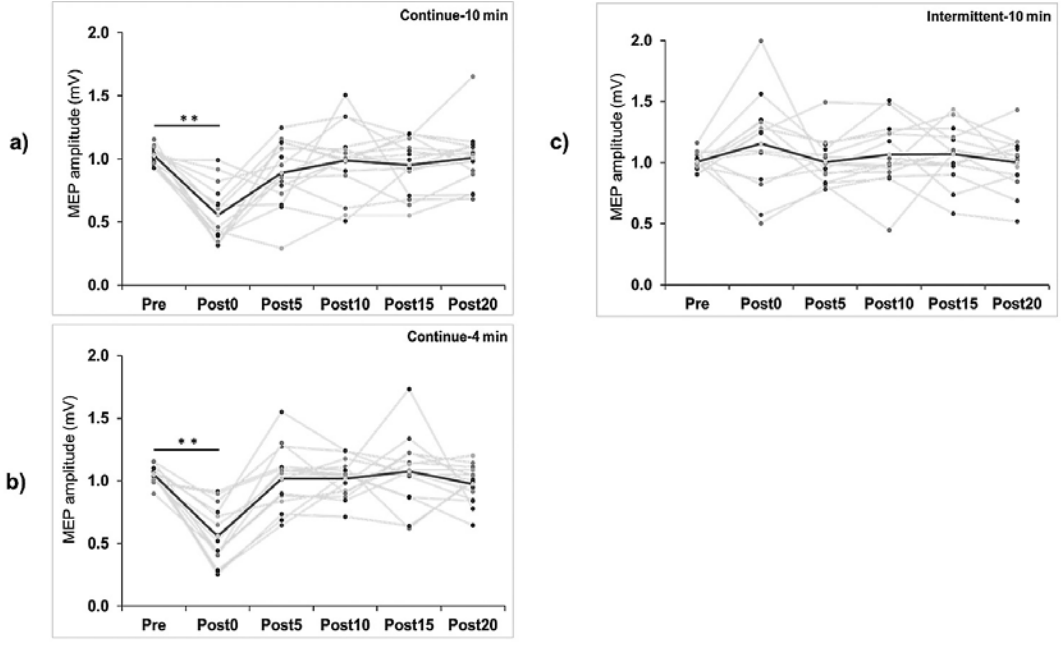

Figure 4. The effects of continuous and intermittent movement tasks on motor evoked potential.
The amplitudes of motor evoked potential (MEP) before and after the three movement task conditions are shown. Compared with baseline values (Pre), the MEP amplitude decreased significantly immediately after the movement task (Post0) in the conditions involving a) continuous abduction at 1 Hz for 10 minutes (Continuous-10 min; $P < 0.01$); and b) continuous abduction at 1 Hz for 4 minutes (Continuous-4 min; $P < 0.01$); c) there was no change in MEP amplitude before and after the movement task in the condition involving intermittent abduction at 1 Hz for 10 minutes (Intermittent-10 min; all $P > 0.05$). ** $P < 0.01$. Post5, 5 minutes after the movement task; Post10, 10 minutes after the movement task; Post15, 15 minutes after the movement task; Post 20, 20 minutes after the movement task.

test was used for post hoc comparisons to compare the amplitudes of MEP before and after TASK. In addition, the Tukey HSD test was also used to test differences among TASK for significance. Statistical significance was set as $P < 0.05$ for all analyses.

Results

The MEP amplitudes in each TASK are shown in Figure 4. The two-way repeated-measures ANOVA demonstrated a significant effect of TASK ($F_{(2,28)} = 4.433$; $P = 0.021$; $\eta 2 = 0.241$) and TIME ($F_{(5,70)} = 12.876$; $P < 0.001$; $\eta 2 = 0.479$) as well as a significant TASKs × TIME interaction ($F_{(10,140)} = 8.730$; $P < 0.001$; $\eta 2 = 0.384$). The post hoc test demonstrated that MEP amplitude at Post0 was significantly lower than that at Pre in the Continuous-10 min ($P < 0.01$; Figure 4a) and Continuous-4 min ($P < 0.01$; Figure 4b) of TASKs; however, no significant differences were found from Post5 to Post20. In the Intermittent-10 min TASK, no significant differences were found between MEP amplitudes (all $P > 0.05$; Figure 4c). Moreover, Tukey HSD test revealed a significant difference between Intermittent-10 min and Continuous-10 min TASK ($P = 0.016$); however, there was no significant difference between Intermittent-10 min and Continuous-4 min TASK and between Continuous-10 min and Continuous-4 min TASK (all $P > 0.05$).

Discussion

In the present study, the 10% MVC tasks showed that the MEP amplitude immediately decreased after continuous repetitive movements but not after intermittent repetitive movements. In addition, no difference was found in the changes in MEP amplitudes after intermittent repetitive movement. These results suggest that changes in MEP amplitude depend on the preceding movement task pattern.

Findings from a previous study demonstrated that corticospinal excitability decreased for 3 minutes after a low-intensity repetitive movement task [8], and are supported by our results demonstrating an effect of continuous movement conditions on MEP. PED involves changes in excitability of the intracortical inhibitory circuit [8, 10]; therefore, this circuit may have been altered after continuous repetitive movements in the present study. In our study, PED occurred after continuous, but not intermittent, repetitive movements, which suggests that the former may be one of the factors causing PED. However, the degree of PED during the 10% MVC was not different between 4- and 10-min continuous repetitive movements. This finding was consistent with that of a previous study that there was no difference in the change in MEP amplitude between 2- and 6-min tasks [8].

MEP amplitude did not change in the intermittent movement condition, which involved repetitions of 4 seconds of movement and 6 seconds of rest, while participants counted the number of the movements. A previous study found that PED did not occur after movement tasks which required attention or adjustment of movement [27]. Furthermore, other studies have found that short latency afferent inhibition (SAI) and SICI are decreased by attention [28, 29]. In an intermittent movement task that requires participants to attend to the timing and number of movements, excitability of the gamma-aminobutyric acid and cholinergic system inhibitory circuits in M1 may be reduced. These factors may explain why MEP amplitude did not change after the intermittent movement task in our study. However, we did not measure the degree of attention, SAI, or SICI, and are therefore unable to confirm why PED did not occur in the intermittent movement condition; further studies are needed to investigate this.

Previous studies have shown that corticospinal excitability increases after intermittent PES [15-17], whereas those phenomena did not occur under intermittent movement conditions in this study. That is, it is possible that the simple intermittent movement did not lead to the increase in

cortical excitability. The primary somatosensory cortex, premotor cortex, the supplementary motor area, the posterior parietal cortex and the cerebellum play an important role in motor learning, and are closely related to M1 [30-33]. Corticospinal excitability tendency will probably increase when M1 and related regions were simultaneously activated by intermittent movements. Furthermore, complexity of the task is also an extremely important factor [34]. Previous studies have demonstrated that MEP was larger in a series of complex tasks compared with simple finger abduction [35, 36]. In this study, participants in the intermittent movement showed adjusted levels of muscle contraction along with controlling 4 seconds of tasks followed by 6 seconds of rest. We hypothesized that MEP was enhanced with the increase in the difficulty level of tasks in intermittent movements. In the future, we would like to investigate the effect of complexity of tasks on corticospinal excitability.

The present study demonstrated that corticospinal excitability did not decrease after an intermittent repetitive movement task. Findings suggest that PED may occur after continuous repetitive movement patterns, but not those that are intermittent.

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Conflicts of Interest

There are no conflicts of interest to declare.

References

1. Brasil-Neto JP, Pascual-Leone A, Valls-Sole J, et al. Postexercise depression of motor evoked potentials: a measure of central nervous system fatigue. Exp Brain Res. 1993; 93: 181-184.
2. Brasil-Neto JP, Cohen LG, Hallett M. Central fatigue as revealed by postexercise decrement of motor evoked potentials. Muscle Nerve. 1994; 17: 713-719.
3. Samii A, Wassermann EM, Ikoma K, et al. Characterization of postexercise facilitation and depression of motor evoked potentials to transcranial magnetic stimulation. Neurology. 1996; 46: 1376-1382.
4. Liepert J, Kotterba S, Tegenthoff M, et al. Central fatigue assessed by transcranial magnetic stimulation. Muscle Nerve. 1996; 19: 1429-1434.
5. Brasil-Neto JP, Araujo VP, Carneiro CR. Postexercise facilitation of motor evoked potentials elicited by ipsilateral voluntary contraction. Muscle Nerve. 1999; 22: 1710-1712.
6. Balbi P, Perretti A, Sannino M, et al. Postexercise facilitation of motor evoked potentials following transcranial magnetic stimulation: A study in normal subjects. Muscle Nerve. 2002; 25: 448-452.
7. Lentz M, Nielsen JF. Post-exercise facilitation and depression of M wave and motor evoked potentials in healthy subjects. Clin Neurophysiol. 2002; 113: 1092-1098.
8. Miyaguchi S, Kojima S, Kirimoto H, et al. Do differences in levels, types, and duration of muscle contraction have an effect on thedDegree of post-exercise depression? Front Hum Neurosci. 2016; 10: 159.
9. Bonato C, Zanette G, Fiaschi A, et al. Activity-dependent modulation of synaptic transmission in the intact human motor cortex revealed with transcranial magnetic stimulation. Cereb Cortex. 2002; 12: 1057-1062.
10. Teo WP, Rodrigues JP, Mastaglia FL, et al. Post-exercise depression in corticomotor excitability after dynamic movement: A general property of fatiguing and non-fatiguing exercise. Exp Brain Res. 2012; 216: 41-49.
11. Miyaguchi S, Onishi H, Kojima S, et al. Corticomotor excitability induced by anodal tran-

scranial direct current stimulation with and without non-exhaustive movement. Brain Res. 2013; 1529: 83-91.
12. Baumer T, Munchau A, Weiller C, et al. Fatigue suppresses ipsilateral intracortical facilitation. Exp Brain Res. 2002; 146: 467-473.
13. Bridoux A, Creange A, Sangare A, et al. Impaired sleep-associated modulation of post-exercise corticomotor depression in multiple sclerosis. J Neurol Sci. 2015; 354: 91-96.
14. Teo WP, Rodrigues JP, Mastaglia FL, et al. Changes in corticomotor excitability and inhibition after exercise are influenced by hand dominance and motor demand. Neuroscience. 2012; 210: 110-117.
15. Andrews RK, Schabrun SM, Ridding MC, et al. The effect of electrical stimulation on corticospinal excitability is dependent on application duration: a same subject pre-post test design. J Neuroeng Rehabil. 2013; 10: 51.
16. Chipchase LS, Schabrun SM, Hodges PW. Corticospinal excitability is dependent on the parameters of peripheral electric stimulation: A preliminary study. Arch Phys Med Rehabil. 2011; 92: 1423-1430.
17. Chipchase LS, Schabrun SM, Hodges PW. Peripheral electrical stimulation to induce cortical plasticity: A systematic review of stimulus parameters. Clin Neurophysiol. 2011; 122: 456-463.
18. Ridding MC, Brouwer B, Miles TS, et al. Changes in muscle responses to stimulation of the motor cortex induced by peripheral nerve stimulation in human subjects. Exp Brain Res. 2000; 131: 135-143.
19. Ridding MC, McKay DR, Thompson PD, et al. Changes in corticomotor representations induced by prolonged peripheral nerve stimulation in humans. Clin Neurophysiol. 2001; 112: 1461-1469.
20. Mima T, Oga T, Rothwell J, et al. Short-term high-frequency transcutaneous electrical nerve stimulation decreases human motor cortex excitability. Neurosci Lett. 2004; 355: 85-88.
21. Schabrun SM, Ridding MC, Galea MP, et al. Primary sensory and motor cortex excitability are co-modulated in response to peripheral electrical nerve stimulation. PLoS One. 2012; 7: e51298.
22. Murakami T, Sakuma K, Nomura T, et al. Short-interval intracortical inhibition is modulated by high-frequency peripheral mixed nerve stimulation. Neurosci Lett. 2007; 420: 72-75.
23. Huang YZ, Edwards MJ, Rounis E, et al. Theta burst stimulation of the human motor cortex. Neuron. 2005; 45: 201-206.
24. Miyaguchi S, Kojima S, Sasaki R, et al. Decrease in short-latency afferent inhibition during corticomotor postexercise depression following repetitive finger movement. Brain Behav. 2017; 7: e00744.
25. Rawji V, Ciocca M, Zacharia A, et al. tDCS changes in motor excitability are specific to orientation of current flow. Brain Stimul. 2018; 11: 289-298.
26. Tsuiki S, Sasaki R, Pham MV, et al. Repetitive passive movement modulates corticospinal excitability: effect of movement and rest cycles and subject attention. Front Behav Neurosci. 2019; 13: 38.
27. Ishikawa N, Miyao R, Tsuiki S, et al. Corticospinal excitability following repetitive voluntary movement. Journal of Clinical Neuroscience. 2018.
28. Mirdamadi JL, Suzuki LY, Meehan SK. Attention modulates specific motor cortical circuits recruited by transcranial magnetic stimulation. Neuroscience. 2017; 359: 151-158.
29. Thomson RH, Garry MI, Summers JJ. Attentional influences on short-interval intracortical inhibition. Clin Neurophysiol. 2008; 119: 52-62.
30. Rocco-Donovan M, Ramos RL, Giraldo S, et al. Characteristics of synaptic connections be-

tween rodent primary somatosensory and motor cortices. Somatosensory & motor research. 2011; 28: 63-72.
31. Park JW, Kim YH, Jang SH, et al. Dynamic changes in the cortico-subcortical network during early motor learning. NeuroRehabilitation. 2010; 26: 95-103.
32. Grafton ST, Hazeltine E, Ivry R. Functional mapping of sequence learning in normal humans. J Cogn Neurosci. 1995; 7: 497-510.
33. Doyon J, Penhune V, Ungerleider LG. Distinct contribution of the cortico-striatal and cortico-cerebellar systems to motor skill learning. Neuropsychologia. 2003; 41: 252-262.
34. Kennefick M, Burma JS, van Donkelaar P, et al. Corticospinal excitability is enhanced while preparing for complex movements. Exp Brain Res. 2019; 237: 829-837.
35. Flament D, Goldsmith P, Buckley CJ, et al. Task dependence of responses in first dorsal interosseous muscle to magnetic brain stimulation in man. J Physiol. 1993; 464: 361-378.
36. Roosink M, Zijdewind I. Corticospinal excitability during observation and imagery of simple and complex hand tasks: Implications for motor rehabilitation. Behav Brain Res. 2010; 213: 35-41.