

Corticospinal excitability during motor imagery is diminished by continuous repetition-induced fatigue

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Abstract

Application of continuous repetition of motor imagery can improve the performance of exercise tasks. However, there is a lack of more detailed neurophysiological evidence to support the formulation of clear standards for interventions using motor imagery. Moreover, identification of motor imagery intervention time is necessary because it exhibits possible central fatigue. Therefore, the purpose of this study was to elucidate the development of fatigue during continuous repetition of motor imagery through objective and subjective evaluation. The study involved two experiments. In experiment 1, 14 healthy young volunteers were required to imagine grasping and lifting a 1.5-L plastic bottle using the whole hand. Each participant performed the motor imagery task 100 times under each condition with 48 hours interval between two conditions: 500 mL or 1500 mL of water in the bottle during the demonstration phase. Mental fatigue and a decrease in pinch power appeared under the 1500-mL condition. There were changes in concentration ability or corticospinal excitability, as assessed by motor evoked potentials, between each set with continuous repetition of motor imagery also under the 1500-mL condition. Therefore, in experiment 2, 12 healthy volunteers were required to perform the motor imagery task 200 times under the 1500-mL condition. Both concentration ability and corticospinal excitability decreased. This is the first study to show that continuous repetition of motor imagery can decrease corticospinal excitability in addition to producing mental fatigue. This study was approved by the Institutional Ethics Committee at the Nagasaki University Graduate School of Biomedical and Health Sciences (approval No. 18121302) on January 30, 2019.

Key Words: central nervous system; concentration; continuous repetition of motor imagery; corticospinal excitability; mental fatigue; motor evoked potential; motor imagery; muscle fatigue; neurophysiology; transcranial magnetic stimulation

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Introduction

Motor imagery is the act of mentally simulating a movement without any actual movement or muscle activity (Jeannerod, 1995; Decety, 1996). Neurophysiologically, brain activation overlaps during motor imagery and actual motion (Héту et al., 2013). Transcranial magnetic stimulation (TMS) studies have demonstrated an increase in M1 excitability during imagery of target muscle contraction using motor evoked potentials (MEPs) (Kasai et al., 1997; Yahagi and Kasai, 1998). In addition, continuous repetition of motor imagery is expected to improve the performance of motor tasks. Multiple randomized controlled trials have reported amelioration of motor paralysis of upper limb function after stroke (Page et al., 2009, 2011), and systematic reviews have also shown the effectiveness of motor imagery (Langhorne et al., 2009; Hatem et al., 2016). However, these studies used different intervention times and frequencies (Malouin et al., 2013; Guerra et al., 2017). In particular, Ruffino et al. (2017a) have highlighted the importance of intervention time in effective motor imagery.

Physical practice is generally considered an effective treatment for paralysis after stroke; more is better in terms of amount and frequency while considering important factors such as risk management and fatigue (Cumming et al., 2011; Sterr et al., 2002; Bernhardt et al., 2016; Winstein et al., 2016). This implies that motor imagery could also be similarly beneficial; however, it is necessary to investigate the fatigue component of continuous repetition of motor imagery to consider the amount and frequency that is needed to provide benefit. There are no studies reporting a definite relationship between continuous repetition of motor imagery and fatigue. One previous study has demonstrated decreased muscle endurance 3 minutes after a hand-grip-endurance motor imagery task (Graham et al., 2014). Another study has reported that continuous repetition of motor imagery causes mental fatigue (Rozand et al., 2014), which has been shown to affect performance (Rozand et al., 2016). More detailed evidence including neurophysiological findings associated with the development of central fatigue after continuous repetition of motor imagery is needed.

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In this study, we aimed to elucidate this phenomenon through subjective and objective assessments to help design an effective motor imagery task involving grasping and lifting of a 1.5-L plastic bottle with the whole hand.

Subjects and Methods

This is an experimental study. Subjects were recruited via study advertisement in the Nagasaki University. This study involved experiments 1 and 2. The weight of the object used during actual motion could influence the appearance of fatigue associated with motor imagery, the motor imagery task was executed 100 times under each condition in experiment 1: the bottle contained either 500 mL or 1500 mL of water during the demonstration phase. The two conditions were executed by the same participants, and the second condition was performed 48 hours after the first. Subsequently, in experiment 2, the motor imagery task was conducted 200 times in the 1500-mL condition and the effect of the continuous repetition of motor imagery was examined. This study was approved by the Institutional Ethics Committee at the Nagasaki University Graduate School of Biomedical and Health Sciences (approval No. 18121302) on January 30, 2019. All experimental procedures were conducted in accordance with the Declaration of Helsinki (World Medical Association, 2013) and its later amendments.

Experiment 1

Participants

Fourteen healthy volunteers (8 men and 6 women, mean age 26 ± 4.6 years) were enrolled. None of the study participants had a history of major physical disorders, including neurological illness, brain injury, or psychiatric illnesses.

Motor imagery ability assessment

All participants completed the Movement Imagery Questionnaire-Revised (MIQ-R) (Hall and Martin, 1997) at the beginning of the experiment. The MIQ-R assesses a participant's ability to see (visual imagery) and feel (kinesthetic imagery) different movements. This instrument consists of eight separate movement items (four visual and four kinesthetic). After performing and imagining the movement, the participants rated their imagery using a seven-point Likert Scale (1 = very hard to see/feel; 4 = neutral (not easy/not hard); 7 = very easy to see/feel). Their motor imagery ability was evaluated based on the total score; the higher the MIQ-R total score, the higher the motor imagery ability.

Motor imagery task

Participants underwent motor imagery demonstration and execution on a reclining chair with both hands on a table. The motor imaging task was performed based on a previous study (Alaerts et al., 2010). To maintain clarity during motor imagery, an action common in activities of daily living was chosen (i.e., grasping and lifting a 1.5-L plastic bottle). In the demonstration phase, participants were instructed to reach and grasp an actual 1.5-L plastic bottle containing either 500 mL or 1500 mL of water and subsequently lifted it to place on a 10 cm high stand in 2 seconds. During the motor imagery task, the participants were instructed to imagine performing this movement. Specifically, they were asked to imagine the (kinesthetic) experience of the movement (rather than a visual type of imagery), to remain relaxed, and to avoid movements during the motor imagery task.

Subjective assessment

Mood evaluation was conducted using the Profile of Mood

States, Second Edition (POMS2) (Heuchert and McNair, 2012). POMS2 consists of 65 questions and six subscales, namely Anger-Hostility (AH), Confusion-Bewilderment (CB), Depression-Dejection (DD), Fatigue-Inertia (FI), Tension-Anxiety (TA), Vigor-Activity (VA), and Friendliness (F), which are further assessed to provide Total Mood Disturbance (TMD). The response to each question is recorded on a 5-point Likert scale ranging from "0 = not at all" to "4 = extremely," and it takes approximately 10 minutes to respond to all questions. Participants were instructed to respond according to "how I feel right now." The ability to concentrate was assessed using a Visual Analog Scale (VAS). The participants were instructed to draw a line with a length between 0 and 100 mm to show the degree to which they were currently able to concentrate (0 mm = "I cannot concentrate at all," 100 mm = "I can concentrate well"). Fatigue was evaluated on a Likert scale (1 = not tired at all to 7 = very tired).

Objective assessment

Objective evaluation assessed pinch force using a hydraulic pinch gauge (SH-5005, Sakai Medical, Japan) and MEP amplitudes evoked by TMS. In the pinch force evaluation, participants were asked to apply force at maximal voluntary contraction (MVC) for 2 seconds.

TMS and MEP recordings

Surface electromyography (EMG) activity was recorded in the abductor pollicis brevis muscle (APB) using a pair of Ag-AgCl cup electrodes of 9-mm diameter (SDC112, GE Healthcare, Osaka, Japan). Surface EMG signals were amplified and filtered at a bandwidth of 5–3000 Hz using a digital signal processor (Neuropack Sigma MEB-5504, Nihon Kohden, Tokyo, Japan), and transferred to a computer for off-line analysis after passage through an A/D converter at a sampling frequency of 2 kHz (PowerLab 16/30, AD Instruments, Sydney, Australia).

TMS used a figure-of-eight coil (7 cm coil diameter) connected to a magnetic stimulator (Magstim 200, Magstim, Whitland, UK). First, we identified the optimal TMS coil position for evoking MEPs in the right APB (the hotspot). Next, we marked the coil position on a swimming cap covering the scalp of each participant. The coil was placed tangentially to the scalp with its handle pointing backward and at an angle of approximately 45° from the mid-sagittal line. Attention was taken to maintain the same coil position relative to the scalp throughout the experiments. The resting motor threshold (MT) was defined as the lowest stimulus intensity that evoked an MEP of at least 50 μ V in the right APB in five out of 10 trials. The test stimulus intensity was then set at 110–130% of the resting MT. The mean size of the control MEPs for the APB was approximately 0.5–1.0 mV. Throughout the experiments, participants were instructed to avoid inadvertent movements that could lead to background EMG activity. For each trial, a 20-ms period preceding the TMS trigger was visually inspected for any background EMG activity.

Timing of TMS

A computerized pulse-generation system (LabView, National Instruments, Austin, TX, USA) was used to control the timing of TMS during the motor imagery task. One 4-minute task set consisted of 20 sessions, and one motor imagery session lasted 12,000 ms. The participants performed the experiment with their eyes closed to facilitate concentrating on the imagery. Thus, the motor imagery task was controlled by two sounds: a session started with a warning signal and a start signal was delivered 5000 ms later. The task was executed during the 2000 ms after the start signal. Despite the motor

imagery practice, there remained a possibility of a slight gap in motor imagery timing. To account for this, the TMS had four set timings because it was stimulated with the gripping or lifting phase for the plastic bottle. Therefore, the timings of TMS were randomly controlled using the LabView system at 1200, 1400, 1600, or 1800 ms from the start signal. The participants were instructed to announce when the TMS stimulus clearly occurred outside of the motor imagery task by raising one hand.

Experimental procedure

The participants were evaluated by POMS2 and pinch force and were assigned to the two tasks by a counterbalanced design. Additionally, in the pinch force task, participants were asked to apply force at MVC for 2 seconds. Next, the motor imagery task (500 or 1500 mL) was practiced, and the experiment was started after ensuring that the participant was able to imagine the task clearly. The experiment was conducted with the participant in a comfortable posture with both arms resting on a table. Prior to the experimental condition, the participant's baseline corticospinal excitability was assessed by acquiring 10 MEPs while they passively watched a white-colored fixation cross on a black background in the center of the computer screen to exclude attention bias from the ambient environment. The experimental condition comprised five sets of 20 motor imagery sessions, and concentration power was evaluated after each set by VAS. MEPs were measured 100 times during the task, and POMS2 and pinch force were measured before and after each task of five sets (**Figure 1**). The same participants performed the 500 mL-condition and the 1500 mL-condition motor imagery task, with a 48 hour interval between performing the first and second conditions.

Data analysis

Trials with background EMG activity greater than 20 μ V were eliminated from the analysis. MEP amplitude (peak-to-peak) was measured from the APB in every trial. The data were statistically analyzed by *t*-test to investigate the effect of differences in motor-imagery tasks (500 mL vs. 1500 mL) on the POMS2 subscales and pinch force. The MEP data were statistically analyzed using a one-way analysis of variance (ANOVA) with the variable "set number" to investigate whether the absolute MEP amplitude was modulated compared with rest, followed by Dunnett's *post hoc* analysis for multiple comparisons. Next, MEP amplitude was analyzed using peak-to-peak values and expressed as a percentage of the mean amplitude under control conditions. Two-way ANOVA was performed with the variables "weight" and "set" to evaluate the changes in relative MEPs and VAS scores associated with the continuous repetition of motor imagery. In all analyses, the threshold for statistical significance was $P < 0.05$. All analyses were performed using statistical analysis software (SPSS version 22.0, IBM, Armonk, NY, USA).

Experiment 2

Since repetition of the motor imagery for 100 times did not show the development of central fatigue, experiment 2 was designed to repeat the motor imagery task for 200 times using the 1500-mL condition.

Participants

Twelve healthy volunteers (9 men and 3 women, mean age 26 ± 4.9 years) were enrolled in this second phase of the study. Six subjects participated in both experiments.

Experimental procedure

The motor imagery task used the 1500-mL condition in 10 sets, with 20 sessions in each set. TMS stimulation was administered 10 times per set and randomly controlled by the LabView system. The experimental procedure was carried out in accordance with that of experiment 1, only VAS was used for subjective evaluation, and TMS and pinch force were used for objective evaluation. The task comprised 200 motor imagery sessions and 100 TMS stimuli.

Data analysis

Pinch force was statistically analyzed by paired *t*-test. One-way ANOVA was performed with the variable "set" to investigate the changes in relative MEP and VAS associated with the continuous repetition of motor imagery, followed by Dunnett's *post hoc* analysis for multiple comparisons. In addition, the absolute MEP data were statistically analyzed using a one-way ANOVA with the variable "set number" to investigate whether the MEP amplitude was modulated compared with rest, followed by Dunnett's *post hoc* analysis for multiple comparisons.

Results

Experiment 1

Motor imagery ability of participants

The mean motor imagery ability of the participants was 49.6 ± 5.6 (kinesthetic imagery: 25.2 ± 3.1 , visual imagery: 24.4 ± 2.9).

Changes in subjective scale scores during motor imagery tasks with different muscle outputs

Mood states revealed AH ($t_{(13)} = 1.98, P = 0.069$), CB ($t_{(13)} = 0.54, P = 0.598$), DD ($t_{(13)} = 1.10, P = 0.29$), FI ($t_{(13)} = 1.98, P = 0.069$), TA ($t_{(13)} = 0.20, P = 0.84$), VA ($t_{(13)} = 1.83, P = 0.089$), F ($t_{(13)} = 0.67, P = 0.513$) and TMD ($t_{(13)} = 1.10, P = 0.289$) were not significantly different in the 500-mL condition with POMS2. In the 1500-mL condition, no significant difference was observed in AH ($t_{(13)} = 1.02, P = 0.328$), CB ($t_{(13)} = 0.71, P = 0.488$), DD ($t_{(13)} = 1.44, P = 0.173$), TA ($t_{(13)} = 0.398, P = 0.697$), F ($t_{(13)} = 1.96, P = 0.072$), however, a statistically significant difference was observed in FI ($t_{(13)} = 2.35, P = 0.035$), VA ($t_{(13)} = 3.80, P = 0.002$), and TMD ($t_{(13)} = 2.50, P = 0.027$) with POMS2. Moreover, the Likert scale indicated significant fatigue in the 1500-mL condition ($t_{(13)} = 3.04, P = 0.009$). Two-way ANOVA did not reveal significant main effects or interactions with concentration, which was evaluated after each set by VAS ("weight," $F_{(1,13)} = 2.671, P = 0.108$; "set" $F_{(4,52)} = 0.227, P = 0.642$; "weight" \times "set" $F_{(4,52)} = 1.168, P = 0.329$).

Changes in objective scale scores during motor imagery task with different muscle outputs

The pinch force did not significantly change in the 500-mL condition ($t_{(13)} = 0.94, P = 0.364$). A significant decrease in muscle strength was observed in the 1500-mL condition ($t_{(13)} = 2.75, P = 0.016$) (**Figure 2**). One-way ANOVA of the absolute MEPs demonstrated a significant main effect for the variable "set number" in the 500-mL condition ($F_{(5,56)} = 5.634, P = 0.001$) and the 1500-mL condition ($F_{(5,56)} = 14.197, P < 0.001$). Dunnett's *post hoc* test revealed a significant increase in MEPs during set 5 in the 500-mL condition ($P = 0.004$), and set 5 in the 1500-mL condition ($P < 0.001$) when compared with rest (**Figure 3**). Next, a two-way ANOVA was performed to investigate the effect of the variables "weight" and "set" on the changes in MEPs associated with the continuous

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repetition of motor imagery. The results showed a significant main effect for “weight” ($F_{(1,13)} = 11.14, P = 0.005$); however, there were no other significant main effects or interactions (“set” $F_{(4,52)} = 0.659, P = 0.623$; “weight” \times “set” $F_{(4,52)} = 0.278, P = 0.891$). These results revealed that the increase in MEP amplitude differed between the 500-mL and 1500-mL conditions.

Experiment 2

Motor imagery ability of participants

The participants’ motor imagery ability was 48.1 ± 6 (kinesthetic imagery: 25.2 ± 1.8 , visual imagery: 22.6 ± 4.6).

Changes in subjective scale scores during motor imagery tasks (200 times)

One-way ANOVA of VAS score demonstrated a main effect ($F_{(9,99)} = 3.797, P = 0.023$). Dunnett’s *post hoc* test indicated a

significant decrease in concentration ability in set 5 ($P = 0.031$), set 7 ($P = 0.032$), set 8 ($P < 0.001$), set 9 ($P = 0.012$), and set 10 ($P = 0.015$; **Figure 4**).

Changes in objective scale scores during motor imagery tasks (200 times)

The pinch force assessment showed a significant decrease in muscle strength ($t_{(11)} = 3.448, P = 0.005$) (**Figure 5**), while one-way ANOVA of MEPs demonstrated a main effect ($F_{(9,99)} = 2.792, P = 0.006$). Dunnett’s *post hoc* test revealed significant decreases in MEPs during set 9 ($P = 0.044$) and set 10 ($P = 0.041$) when compared with set 1 (**Figure 6**). In contrast, one-way ANOVA of the absolute MEPs demonstrated a main effect for the variable “set number” ($F_{(10,110)} = 5.943, P < 0.001$). Dunnett’s *post hoc* test revealed that MEP amplitudes were significantly increased in all conditions, including set 10 ($P = 0.009$), when compared with rest.

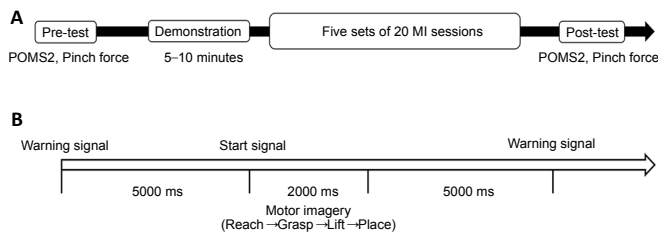


Figure 1 | Experimental design.

(A) Research protocol. (B) A motor imagery session. The motor imagery task consisted of five (experiment 1) or ten (experiment 2) 4-minute sets of 20 sessions each. A session contained one imagined motor performance and lasted 12 seconds. MI: Motor imagery; POMS2: Profile of Mood States, Second Edition.

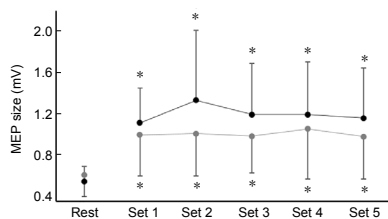


Figure 3 | Change in MEP amplitudes with repetition of motor imagery: experiment 1.

Values are expressed as the absolute MEPs. The absolute MEPs demonstrated significant changes compared with the control condition in both 500-mL condition and 1500-mL condition. Grey line: 500-mL condition. Black line: 1500-mL condition. Data are represented as mean \pm SE. * $P < 0.05$ (one-way analysis of variance followed by Dunnett’s *post hoc* analysis; $n = 14$). MEP: Motor evoked potential.

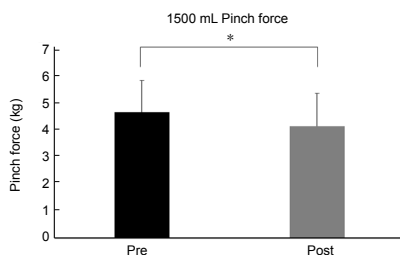


Figure 5 | Pinch force before and after 1500 mL condition: experiment 2. Data are represented as mean \pm SE. * $P < 0.05$ (paired *t*-test; $n = 12$).

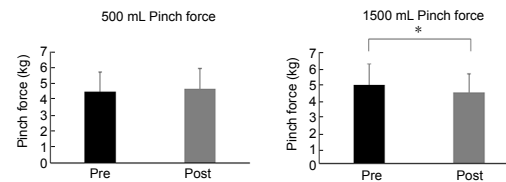


Figure 2 | Pinch force before and after each of the two tasks (500 mL condition or 1500 mL condition): experiment 1.

Pinch force was assessed to examine the influence of muscle power by motor imagery repetition. A significant decrease in muscle strength was observed in the 1500-mL condition. Data are expressed as mean \pm SE. * $P < 0.05$ (paired *t*-test; $n = 14$).

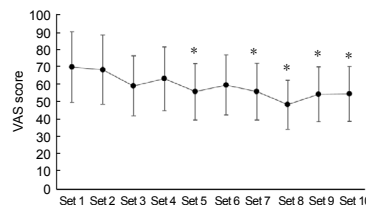


Figure 4 | Change in VAS scores with continuous repetition of motor imagery: experiment 2.

Data are represented as mean \pm SE. * $P < 0.05$ (one-way analysis of variance followed by Dunnett’s *post hoc* analysis; $n = 12$). Sets 1–10 shows each set in experimental 2; VAS: visual analog scale for ability to concentrate.

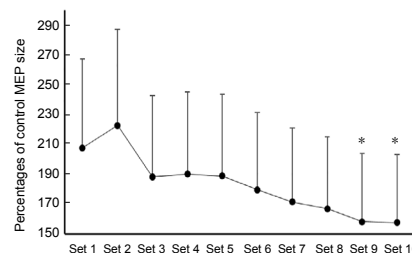


Figure 6 | Change in MEP amplitudes with repetition of motor imagery: experiment 2.

Values are expressed as percentages of the amplitude in the control condition. Data are represented as mean \pm SE. * $P < 0.05$ (one-way analysis of variance followed by Dunnett’s *post hoc* analysis; $n = 12$). Sets 1–10 show each set in experimental 2. MEP: Motor evoked potential.

Discussion

We investigated the process of fatigue that accompanies continuous repetition of motor imagery over time by combining subjective and objective assessments. In the POMS2 subscales, experiment 1 demonstrated TMD and VA deterioration, along with augmentation of FI after continuous repetition of motor imagery in the 1500-mL condition. The pinch force also decreased, but no significant time-dependent changes in VAS scores and MEPs were observed between set 1 and set 5. These results indicated that changes in mood state and pinch force weakness developed after continuous repetition of motor imagery in the 1500-mL condition. However, we hypothesized that the motor imagery sessions were insufficient to cause an MEP decrease associated with fatigue. Thus, in experiment 2, the number of motor imagery sessions was increased to 200 using the 1500-mL condition to investigate the effect of continuous repetition of motor imagery on the central nervous system. Consequently, we established central nervous system changes by continuous repetition of motor imagery and observed a decrease in pinch force as well as decreases in the VAS and MEPs over time.

Significant changes in mood were observed via POMS2 only in the 1500-mL condition. This can be interpreted as evidence of mental fatigue, because it indicates an increase in fatigue and a decrease in vigor with continuous repetition of motor imagery, and agrees with previous studies investigating the relationship between motor imagery and mental fatigue (Rozand et al., 2014, 2016). Mental fatigue develops after prolonged cognitive activity (Boksem and Tops, 2008) and can affect cognitive aspects such as attention (Boksem et al., 2005). While motivation to perform a task may have a strong influence on mental fatigue (Mockel et al., 2015), exogenous motivation in the form of monetary incentives cannot compensate for its effects (Gergelyfi et al., 2015). The role of motivation remains unclear. This study assumed that attention and motivation were both similar between the strong and weak muscle output motor imagery conditions. A previous study has shown that enhancement of corticospinal excitability during motor imagery is associated with an increase in the imagined force level (Mizuguchi et al., 2013). Thus, we speculate that the level of imagined muscle output affects mental fatigue. Although mental fatigue and muscle weakness were demonstrated in experiment 1, further investigation is required to ascertain if there is a direct causal relationship between the two.

A significant decrease in MEPs was observed in experiment 2, which indicates a decrease in excitability of the corticospinal tract. Previous studies have shown a decrease in MEPs after muscle fatigue is associated with exercise (Gruet et al., 2013); however, only a few have demonstrated a decrease in MEP amplitude due to motor imagery. Among them, Kluger et al. (2012) observed a significant decrease in MEP amplitude between baseline and 2 minutes after a hand-grip motor imagery task. However, this study did not investigate the change in MEPs over time during motor imagery because it evaluated the physiological state off-line after the motor imagery. In contrast, the present study found progressively decreasing corticospinal tract excitability during motor imagery. This result confirmed that the participants' physical performances deteriorated during the repeated imagination of the motor task. Concentration (Malouin et al., 2013) and clarity (Ruffino et al., 2017b) are both known to be important

factors for the effectiveness of motor imagery. Accordingly, we used a VAS to evaluate concentration and observed a significant decrease that occurred earlier than the MEP decrease. A review has reported the relationship between increased corticospinal excitability and imagination of the motor action (Grosprêtre et al., 2016); therefore, we propose that reduced concentration decreases corticospinal excitability because it affects the imagination of the motor action.

In addition, we observed a decrease in pinch force after the 1500-mL condition in experiments 1 and 2. An earlier study that investigated the relationship between motor imagery and muscle strength reported no changes in MVCs in elbow flexor muscles before and after an experiment that consisted of 80 intermittent maximum imagined contractions of the elbow flexor muscles (Rozand et al., 2014). However, Graham et al. (2014) demonstrated a decrease in muscle endurance and an increase in EMG amplitude of the flexor carpi ulnaris muscle after 3 minutes of a handgrip endurance imagery task with an imagined 50% MVC. Muscle fatigue may arise not only because of peripheral changes at the level of the muscle, but also because the central nervous system fails to drive the motor neurons adequately; that is, central fatigue develops, causing motor unit firing rates to decline (Gandevia et al., 2001). We observed a significant decrease in MEP amplitudes, which indicated changes in the CNS, suggesting that decreased excitability of the corticospinal tract is a component of central fatigue that decreases muscle strength. Therefore, care should be taken when performing motor imagery training for motor imagery tasks with strong muscle exertion. However, the relationship between motor imagery and muscle fatigue should be investigated further, as many unclear points remain.

The study has some limitations. First, it focused on a task resembling a common activity of daily living to maintain clarity during motor imagery. Thus, for each participant, the motor imagery task had a respectively different feel regarding the weight of the object. The effect of fatigue on continuous repetition of motor imagery should be examined in future studies using a task that standardizes muscle exertion in participants. Second, this study did not assess corticospinal excitability at rest at the end of the motor imagery session. Therefore, changes in corticospinal excitability before and after motor imagery could not be confirmed. Third, the sample size was relatively small. Future studies are necessary on larger, appropriately calculated sample sizes. Finally, there was a discrepancy between the timing of APB muscle contraction and the timing of TMS. Thus, these experiments were conducted after sufficient practice in timing the contraction of APB muscles and that of TMS.

In conclusion, this study shows that the development of fatigue over time due to continuous repetition of motor imagery is distinct and depends on difference in muscle exertion during the actual movement. Furthermore, repetition of motor imagery decreases the excitability of the corticospinal tract in addition to producing a mental fatigue. The results of this study may help establish a motor imagery training protocol for future studies. However, it should be noted that the fatigue resulting from continuous repetition of motor imagery we observed is specific to the task and the participants. It is likely that different results would be observed among older participants and patients. Accordingly, further studies are needed to establish a motor imagery training protocol.

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Author contributions: AN, TM, KS, TH, and KS conceived and designed the experiments. AN, DM, KA, and TH performed the experiments. AN, TM, TH, and TH analyzed the data. AN, JN, and TS designed the experiment program. AN and TH wrote the article. All authors approved the final version of this paper for publication.

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Declaration of participant consent: The authors certify that they have obtained all appropriate participant consent forms. In the form, the participants have given their consent for their images and other clinical information to be reported in the journal. The participants understand that their names and initials will not be published and due efforts will be made to conceal their identity.

Reporting statement: This study followed the STrengthening the Reporting of OBServational studies in Epidemiology (STROBE) statement.

Biostatistics statement: The statistical methods of this study were reviewed by the biostatistician of Toshio Higashi, Nagasaki University in Japan.

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