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RESEARCH ARTICLE

Time course of changes in corticospinal excitability induced by motor imagery during action observation combined with peripheral nerve electrical stimulation

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Abstract

While previous studies assessed corticospinal excitability changes during and after motor imagery (MI) or action observation (AO) combined with peripheral nerve electrical stimulation (ES), we examined, for the first time, the time course of corticospinal excitability changes for MI during AO combined with ES (AO–MI + ES) using transcranial magnetic stimulation to measure motor evoked potentials (MEPs) in healthy individuals. Fourteen healthy volunteers participated in the following three sessions on different days: AO–MI alone, ES alone, and AO–MI + ES. In the AO–MI task, participants imagined squeezing and relaxing a ball, along with the respective actions shown in a movie, while passively holding the ball. We applied ES (intensity, 90% of the motor threshold) to the ulnar nerve at the wrist, which innervates the first dorsal interosseous (FDI) muscle. We assessed the FDI muscle MEPs at baseline and after every 5 min of the task for a total of 20 min. Additionally, participants completed the Vividness of Movement Imagery Questionnaire-2 (VMIQ-2) at the beginning of the experiment. Compared to baseline, AO–MI + ES significantly increased corticospinal excitability after 10 min, while AO–MI or ES alone had no effect on corticospinal excitability after 20 min. Moreover, the AO–MI + ES-induced cortical excitability changes were correlated with the VMIQ-2 scores for visual and kinaesthetic imagery. Collectively, our findings indicate that AO–MI + ES induces cortical plasticity earlier than does AO–MI or ES alone and that an individual's imagery ability plays an important role in inducing cortical excitability changes following AO–MI + ES.

Keywords Motor imagery · Action observation · Peripheral nerve electrical stimulation · Neural plasticity · Rehabilitation

Introduction

Therapeutic induction and guidance of synaptic plasticity play fundamental roles in functional motor recovery in patients after stroke (Ward and Cohen 2004). Cortical excitation and sensory input can be used to induce plasticity during neurorehabilitation (Stefan et al. 2000; Wolters et al. 2003; Yamaguchi et al. 2016).

One of the rehabilitative methods used in clinical settings is voluntary contraction (VC) combined with peripheral nerve electrical stimulation (ES), which induces plasticity and improves motor skills in patients after stroke as well as in healthy individuals (Chipchase et al. 2011; de Kroon et al. 2005; Khaslavskaia and Sinkjaer 2005; Ridding et al. 2000; Sugawara et al. 2014; Takahashi et al. 2017, 2018; Yamaguchi et al. 2012). These studies reported that ES during VC promotes corticospinal excitability and plastic changes of the motor cortex and spinal circuits in response

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to the alterations of afferent input generated using ES. However, VC combined with ES is not suitable for individuals after severe hemiparetic stroke because of the limitations associated with motor paralysis. Thus, the development of new methods for enhancing plasticity and improving motor function in individuals following severe hemiparetic stroke is sorely needed.

As an alternative to VC, motor imagery (MI), defined as the mental execution of an action without any physical movement or muscle activation (Jeannerod 1995), can be employed to induce plasticity and motor function recovery after stroke (Abbas et al. 2011; Braun et al. 2006; de Vries and Mulder 2007; Facchini et al. 2002; Yahagi et al. 1996). Likewise, action observation (AO), defined as a dynamic state during which an observer can understand what other people are doing by simulating the actions and outcomes that are likely to follow from the observed motor act (Keysers and Gazzola 2010), has the potential to promote motor function recovery following stroke (Bisio et al. 2015a, b, 2017; Eaves et al. 2016; Vogt et al. 2013). In addition, the increase in corticospinal excitability (Eaves et al. 2016; Mouthon et al. 2015; Wright et al. 2014) and brain activation (Berends et al. 2013; Eaves et al. 2016; Nedelko et al. 2012; Villiger et al. 2013; Vogt et al. 2013) with AO–MI is higher than with MI or AO alone. Therefore, AO–MI may exhibit an enhanced ability to induce cortical plasticity than when used individually as a single strategy.

Research has shown that the corticospinal excitability induced using MI combined with ES is higher than that induced using ES alone in healthy individuals (Bonassi et al. 2017; Kaneko et al. 2014; Saito et al. 2013; Yamaguchi et al. 2012) and may improve motor function after stroke (Hong et al. 2012). Additionally, AO combined with ES induces an increase in the corticospinal excitability that lasts for up to 45 min after a combined task in healthy individuals (Bisio et al. 2015a, b). Although previous studies (Bisio et al. 2015a, b, 2017; Kaneko et al. 2014; Saito et al. 2013; Yamaguchi et al. 2012) focused on the changes in cortical excitability that occurred during and after MI or AO plus ES, to the best of our knowledge, no study has examined the intervention timeframe of MI during AO combined with ES (AO–MI + ES) needed to induce cortical plasticity changes in healthy individuals. This type of investigation has clinical implications for the application of AO–MI + ES in the rehabilitation of individuals with severe hemiparetic stroke. Therefore, the aims of the present study conducted in healthy individuals were: (1) to examine the incremental effects of AO–MI + ES repetition on cortical plasticity using transcranial magnetic stimulation (TMS) to measure motor evoked potentials (MEPs); and (2) to test the relationship between vividness of imagery and the task-induced MEP changes. We hypothesised that AO–MI + ES would induce cortical plasticity, with earlier induction than AO–MI or ES alone (Bisio et al. 2015a, b, 2017; Bonassi et al. 2017; Kaneko et al. 2014; Saito et al. 2013; Yamaguchi et al. 2012). In addition, we hypothesised that the vividness of participants' imagery prior to the tasks would influence the changes in corticospinal excitability induced by AO–MI alone and AO–MI + ES (Williams et al. 2012).

Materials and methods

All participants provided written informed consent prior to participation. The project protocol (approval number: 25) was approved by the Ethical Review Board of Tokyo Bay Rehabilitation Hospital in Japan and conformed to the tenets of the Declaration of Helsinki.

Participants

14 healthy volunteers (8 women) aged 22–30 years [mean ± standard deviation (SD), 25 ± 2 years] participated in this study. All participants were right handed, as confirmed with the Edinburgh Inventory (Oldfield 1971). None of the participants had a history of any neurological disease, or were receiving any acute or chronic medication that may affect the central nervous system. The sample size was based on a previous study (Bonassi et al. 2017). This study reported that the AO + ES group consisting of 12 participants showed increased motor cortical excitability following 15 min of training. To obtain a higher number of participants than that in a previous study, 14 participants were recruited in the present study. Volunteers participated in the following three separate sessions that were randomly administered on different days: MI during AO (AO–MI) alone, ES alone, and AO–MI combined with ES (AO–MI + ES). The sessions were separated by at least 3 days to prevent carry-over effects from the previous interventions. The reason for administering the interventions in a random order was that this study was an experimental study with no fixed number of participants. Participants were unaware of the hypothesis, although they were explained that the experiment was conducted to investigate the combined effects of AO–MI and ES on MEPs. Participants performed four sets of the task (5 min per set, total 20 min) during each session. They were administered TMS immediately after the task to investigate the incremental effects of task repetition (AO–MI alone, ES alone, and AO–MI + ES) on corticospinal excitability. The MEPs and resting motor thresholds (RMTs) were assessed at baseline (T0), and after one set (T5), two sets (T10), three sets (T15), and four sets (T20) of the task (Fig. 1).

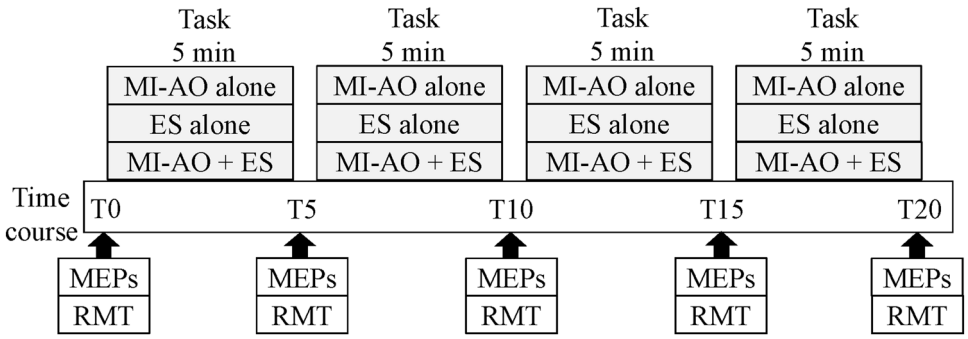

Fig. 1 Experimental protocol. 14 healthy volunteers participated in the following three sessions on different days: (1) motor imagery during action observation (AO–MI), (2) peripheral nerve electrical stimulation (ES) alone, and (3) AO–MI + ES. During each session, we measured the motor evoked potentials (MEPs) and the resting motor threshold (RMT) at baseline (T0) and 5 min (T5), 10 min (T10), 15 min (T15), and 20 min (T20) after the start of the task

Motor imagery during action observation

Participants sat comfortably on a chair with their right forearms positioned horizontally over a table (Fig. 2). They were instructed to put their right arm into a box on a table and to watch a personal computer monitor that was placed on the box. The right hand held a soft ball (diameter = 4 cm). The monitor projected a short live movie clip (5 s) that showed a hand squeezing the ball. The movie involved the action of squeezing for 2 s and relaxing for 3 s. Participants were asked to imagine squeezing and relaxing of the ball, along with the respective actions in the movie, while passively holding the ball (Mizuguchi et al. 2012). To confirm muscle contraction during the task, we carefully checked the electromyogram (EMG) of the first dorsal interosseous (FDI) muscle. In addition, to assess the participants' ability to visually and kinaesthetically imagine a variety of movements, all participants completed the Vividness of Movement Imagery Questionnaire-2 (VMIQ-2) (Roberts et al. 2008) at the beginning of the experiment. The VMIQ-2 requires participants to imagine themselves performing 12 actions from the following three imagery perspectives: internal visual imagery (first-person perspective), external visual imagery (third-person perspective), and kinaesthetic imagery (feeling the movement). For internal visual imagery, one imagines performing a movement. For external visual imagery, one imagines him/herself performing a movement with an external/third-person view of his or her body. For kinaesthetic imagery, one imagines how the movement feels. Participants rated the vividness of each imagery type using a 5-point scale; the scores related to each of the 12 actions were summed to provide a vividness score for each imagery type that ranged from 12 to 60, with lower scores indicating more-vivid imagery.

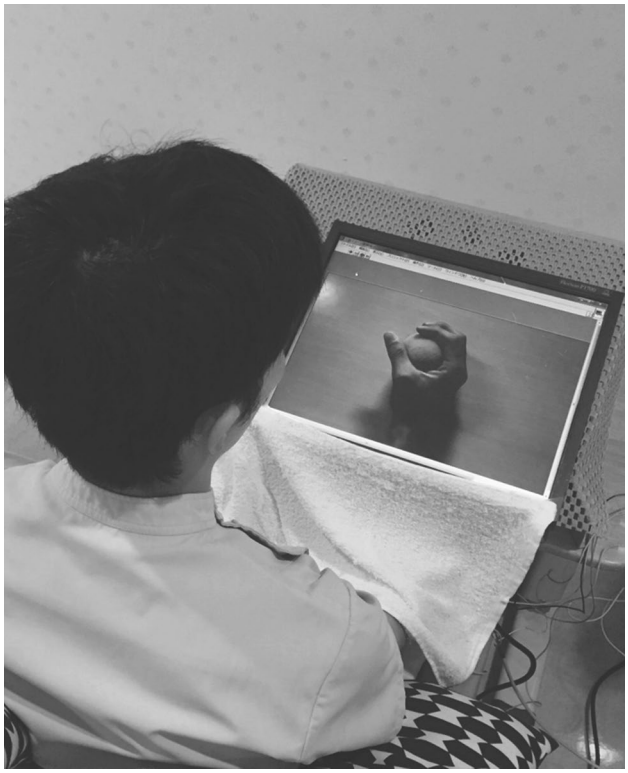

Fig. 2 Environmental setting of the motor imagery and action observation task. The participants were instructed to place their right arm into a box that was positioned on a table and to watch a computer monitor that was placed on top of the box. The right hand held a soft ball (4 cm in diameter), and the monitor projected a short live movie clip (5 s) that showed a hand squeezing the ball. The movie involved actions of squeezing for 2 s and relaxing for 3 s. Participants were asked to imagine squeezing and relaxing the ball, along with the respective actions of the hand shown in the movie, while passively holding the ball

Peripheral nerve electrical stimulation

We delivered ES to the right ulnar nerve, which innervates the FDI muscle, at the wrist, with trains of 20 10-Hz pulses (pulse width = 1 ms) (Yamaguchi et al. 2012) and on–off repetitions of 5 s (on: 2 s, off: 3 s) using Neuropack MEB-2306 (Nihon Kohden, Shinjuku-ku Tokyo, Japan). The intensity was set to 90% of the motor threshold of the FDI muscle that did not induce any finger movement or pain. The motor threshold was defined as the lowest stimulus that evoked visible and tactile twitching of the FDI muscle. The stimulus intensity of ES was 2.49 ± 1.11 mA in the ES task and 1.77 ± 0.48 mA in the AO–MI + ES task.

Electromyogram recording

Participants were seated in a comfortable chair in front of a table, with the forearm positioned horizontally above a pillow and the elbow flexed at an angle of 45° in the pronated position. We recorded the EMGs of the FDI muscle with Ag/AgCl-plated surface electrodes (1-cm diameter) placed at the centre of the muscle belly with a 10-mm inter-electrode distance over the target muscle in the right upper limb. The EMG signal was amplified and band-pass filtered from 10 Hz to 5 kHz using Neuropack MEB-2306 (Nihon Kohden). Signals were recorded at a sampling rate of 5 kHz and stored on the computer for later analysis using the LabVIEW software (National Instruments Inc., Austin, TX, USA).

Corticospinal excitability

To assess changes in corticospinal excitability, we applied a single-pulse stimulation to the primary motor cortex using TMS. The stimulation was delivered through a figure-eight-shaped coil (9-cm diameter loops) connected to a Magstim 200 system (Magstim Co., Whitland, UK). The coil handle was held at a 45° angle to the midsagittal line, approximately perpendicular to the central sulcus. The hotspot of the primary motor cortex was confirmed based on induction of the largest MEP in the FDI muscle at rest. The stimulus intensity was set to evoke MEPs of the FDI muscle with peak-to-peak amplitudes of approximately 1 mV during the resting condition in the beginning of the experiment. This intensity was used throughout the experiment. The MEPs were elicited 15 times at each time with an inter-stimulus interval of 5–7 s. At each time for each task, the MEP response was measured as the peak-to-peak amplitude, and the mean amplitude was calculated. The RMT was also measured; the RMT was defined as the stimulus intensity that evoked reproducible MEPs of more than 100 μV 5 out of 10 times in the FDI muscle at rest. The values (%) are presented as a percentage of the maximum machine output. If the target muscle was not relaxed during the trials, the data were rejected online, and the test condition was repeated.

Statistical analysis

Two-way repeated-measures analyses of variance (ANOVAs) were performed to investigate the effects of "task" (AO–MI alone, ES alone, AO–MI + ES) and "time" (T0, T5, T10, T15, T20) on the MEP amplitudes and RMTs. Dunnett's post hoc multiple comparison tests were used to compare the baseline assessments (T0) to other time points when significant results were obtained in the primary analyses. The effect size (d) for the AO–MI + ES task data for T10, T15, and T20 compared to that at T0 was calculated. To test the hypothesis that the participants' imagery abilities prior to the tasks would influence the changes in corticospinal excitability that were induced by AO–MI alone and AO–MI + ES (Williams et al. 2012), the correlations between the VMIQ-2 scores and significant changes in the MEP amplitude from baseline to several time points (T5, T10, T15, T20) were assessed using Pearson's correlation analyses. The magnitude of change in the MEP amplitude was calculated by subtracting the data obtained at each time point from the baseline data (T0). Statistical significance was set at $p < .05$ for all comparisons. Statistical analyses were performed using SPSS 23.0 (IBM Corp., Armonk, NY, USA) for Windows.

Results

The MEP amplitude values are shown in Table 1. Baseline MEP amplitudes were not significantly different for the three tasks [F (2, 29) = 1.981, p = .152].

Figure 3 shows changes in the mean MEP amplitude and individual dot plot at each time point. A two-way repeated-measures ANOVA of the MEP amplitudes revealed a significant main effect of time [F (4, 52) = 2.902, p = .031], but not task [F (2, 26) = 0.986, p = .387], and a significant interaction [F (8, 104) = 2.084, p = .044]. Post hoc Dunnett's comparisons showed that AO–MI + ES significantly increased the MEP amplitude at T10 (p = .032, d = 1.31), T15 (p = .019, d = 1.37), and T20 (p = .001, d = 1.43) compared to that at T0, while AO–MI alone and ES alone did not change the MEP amplitudes at any time point (Table 1).

The RMT values are shown in Table 1. A two-way repeated-measures ANOVA of the RMTs did not reveal any significant main effects [task: F (2, 26) = 2.602, p = .093; time: F (4, 52) = 0.292, p = .882] or a significant interaction [F (8, 104) = 0.345, p = .946].

The mean (SD) VMIQ-2 scores were 21.6 (7.9), 21.7 (9.6), and 22.9 (9.1) for internal visual imagery, external

Table 1 The motor evoked potential amplitudes and resting motor threshold values at each time point for each task

	T0	T5	T10	T15	T20
MEP (mV)					
AO–MI	1.07 (0.20)	1.11 (0.32)	1.11 (0.33)	1.07 (0.36)	1.00 (0.32)
ES	0.97 (0.26)	1.01 (0.32)	1.03 (0.29)	1.09 (0.38)	1.13 (0.35)
AO–MI + ES	0.91 (0.16)	1.15 (0.28)	1.17 (0.23)*	1.19 (0.24)*	1.28 (0.33)*
RMT (%)					
AO–MI	41.8 (7.0)	41.9 (6.8)	41.9 (6.5)	41.6 (6.7)	41.8 (6.4)
ES	42.1 (6.5)	42.1 (5.8)	42.3 (6.0)	42.4 (6.5)	42.4 (6.1)
AO–MI + ES	40.4 (6.8)	40.9 (6.1)	40.8 (6.6)	40.9 (6.7)	40.9 (6.5)

Data are presented as the mean ± the standard deviation (in parenthesis) at baseline (T0), after one set (T5), after two sets (T10), after three sets (T15), and after four sets (T20) of the task. The RMT values are presented as the percentage of the maximum machine output

AO–MI motor imagery during action observation, *ES* electrical stimulation, *AO–MI + ES* motor imagery during action observation combined with electrical stimulation, *MEP* motor evoked potential, *RMT* resting motor threshold

*$p < .05$ compared to T0 (baseline), as assessed using Dunnett's test

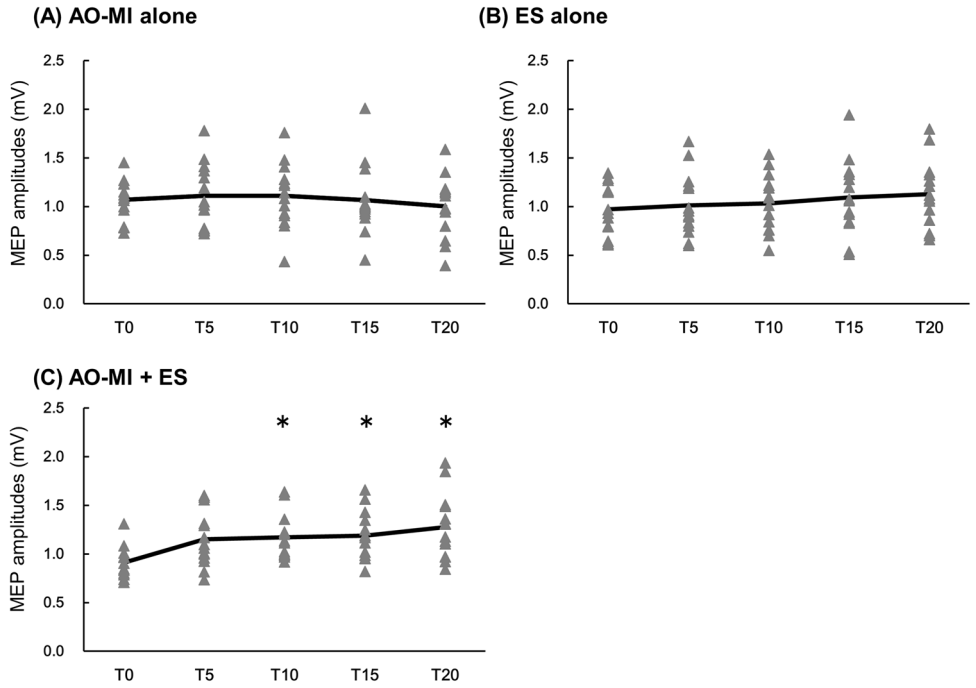

Fig. 3 Individual participant data of motor evoked potentials (MEPs) for the first dorsal interosseous (FDI) muscle before and after motor imagery during action observation (AO–MI), peripheral nerve electrical stimulation (ES) alone, and AO–MI + ES. Black lines represent the mean data. Grey triangles represent the individual participant data. Effects of AO–MI alone (**a**), ES alone (**b**), and AO–MI + ES (**c**) on MEPs. MEPs before the task (T0). MEPs obtained 5 min (T5), 10 min (T10), 15 min (T15), and 20 min (T20) after beginning the task. *$p < .05$ compared to baseline (T0), as assessed by Dunnett's test; the MEPs of the FDI muscle for the AO–MI + ES task increased in amplitude from T10, while no significant MEP changes were observed for the AO–MI alone and ES alone tasks

visual imagery, and kinaesthetic imagery, respectively, at the beginning of the experiment. The results of the correlation analysis are shown in Table 2. Significant negative correlations between the VMIQ-2 scores and the magnitude of change in the MEP amplitude at various time points were found for internal visual imagery (T10: $r = -0.595$, $p = .025$; T15: $r = -0.681$, $p = .007$), external visual imagery (T10: $r = -0.598$, $p = .024$; T15: $r = -0.578$, $p = .03$), and kinaesthetic imagery (T15: $r = -0.559$, $p = .038$) during AO–MI + ES, and for kinaesthetic imagery (T15: $r = -0.603$, $p = .023$) during AO–MI alone. However, no significant correlations between the VMIQ-2 scores and the magnitude of change in the MEP amplitude were noted for ES alone and the other time points.

Table 2 Correlations between the Vividness of Movement Imagery Questionnaire-2 scores and the magnitude of change in the MEP amplitude from baseline

	T5	T10	T15	T20
AO–MI				
Internal visual imagery	− 0.301 (− 0.717 to 0.273)	0.085 (− 0.467 to 0.589)	− 0.474 (− 0.803 to 0.076)	− 0.281 (− 0.706 to 0.293)
External visual imagery	− 0.455 (− 0.794 to 0.010)	− 0.032 (− 0.553 to 0.507)	− 0.377 (− 0.756 to 0.192)	− 0.083 (− 0.588 to 0.468)
Kinesthetic imagery	− 0.408 (− 0.772 to 0.156)	− 0.294 (− 0.713 to 0.280)	− 0.603* (− 0.859 to − 0.106)	− 0.453 (− 0.793 to 0.102)
ES				
Internal visual imagery	− 0.138 (− 0.623 to 0.424)	− 0.275 (− 0.703 to 0.299)	− 0.057 (− 0.570 to 0.488)	− 0.082 (− 0.587 to 0.469)
External visual imagery	− 0.317 (− 0.726 to 0.257)	− 0.352 (− 0.744 to 0.220)	0.001 (− 0.530 to 0.531)	− 0.044 (− 0.561 to 0.498)
Kinesthetic imagery	− 0.074 (− 0.582 to 0.475)	− 0.174 (− 0.645 to 0.393)	0.201 (− 0.369 to 0.661)	0.139 (− 0.423 to 0.624)
AO− MI + ES				
Internal visual imagery	− 0.286 (− 0.709 to 0.288)	− 0.595* (− 0.856 to − 0.094)	− 0.681** (− 0.890 to − 0.236)	− 0.493 (− 0.811 to 0.051)
External visual imagery	− 0.493 (− 0.811 to 0.051)	− 0.598* (− 0.857 to − 0.099)	− 0.578* (− 0.848 to − 0.068)	− 0.169 (− 0.642 to 0.392)
Kinesthetic imagery	− 0.226 (− 0.676 to 0.346)	− 0.404 (− 0.770 to 0.161)	− 0.559* (− 0.840 to − 0.040)	− 0.222 (− 0.673 to 0.350)

Data are presented as the correction coefficient *r* with the upper and lower limits of the 95% confidence interval in parenthesis at baseline (T0), after one set (T5), after two sets (T10), after three sets (T15), and after four sets (T20) of the task

MEP motor evoked potential, *AO–MI* motor imagery during action observation, *ES* electrical stimulation, *AO–MI + ES* motor imagery during action observation combined with electrical stimulation

*$p < .05$, **$p < .01$, as assessed using Pearson's correlation analysis

Discussion

To the best of our knowledge, the present study is the first to provide evidence that AO–MI + ES requires at least 10 min of training time to induce cortical plasticity in healthy individuals. Moreover, the cortical excitability changes that occurred during AO–MI + ES were correlated with the VMIQ-2 scores for visual and kinaesthetic imagery, indicating that imagery ability plays an important role in the induction of cortical excitability changes following AO–MI + ES.

In support of our hypothesis, we found that AO–MI + ES increased cortical excitability earlier than did AO–MI or ES alone. Many reports have indicated that ES alone increases corticospinal excitability and induces cortical plasticity (Chipchase et al. 2011; de Kroon et al. 2005; Khaslavskaia and Sinkjaer 2005; Ridding et al. 2000; Sugawara et al. 2014; Yamaguchi et al. 2012). Research has also shown that AO–MI alone increases corticospinal excitability (Eaves et al. 2016; Mouthon et al. 2015; Wright et al. 2014). Moreover, MI or AO plus ES has been found to increase corticospinal excitability significantly more than either intervention alone (Bisio et al. 2015a, b, 2017; Bonassi et al. 2017; Kaneko et al. 2014; Saito et al. 2013; Yamaguchi et al. 2012). Therefore, AO–MI + ES may have a summative effect; that is, the descending and ascending pathways are both activated during AO–MI + ES, and the increased descending corticospinal volleys during AO–MI + ES may effectively strengthen the corticospinal circuitry more than the individual interventions. The lack of MEP increases following AO–MI or ES alone may be due to the fact that the 20-min task training period used herein was not long enough to increase motor cortex excitability (de Kroon et al. 2005; Khaslavskaia and Sinkjaer 2005; Lafleur et al. 2002; Ridding et al. 2000). Indeed, 15 min of MI or AO–MI did not increase motor cortex excitability (Kaneko et al. 2016; Meng et al. 2018). Thus, future studies should employ longer tasks to address this issue.

The increases in corticospinal excitability that we observed due to repeated exposures to AO–MI + ES were similar to those observed previously for VC combined with ES (Khaslavskaia and Sinkjaer 2005; Sugawara et al. 2014). Neuroimaging studies using functional magnetic resonance imaging showed that the motor-related areas of the brain that are activated during MI are similar to those activated during VC, including the primary motor cortex, supplemental motor area, premotor cortex, parietal region, basal ganglia, and cerebellum (Guillot et al. 2009; Hanakawa et al. 2003, 2008; Imazu et al. 2007; Lacourse et al. 2005; Lotze and Halsband 2006). Additionally, Corbet et al. (2018) reported that MI combined with ES induces desynchronisation over areas of the sensorimotor cortex and enhances the MI-related brain connectivity patterns. Therefore, MI may increase brain activation in a manner similar to VC, while adding sensory input via ES may enhance the ability of the associated brain

networks to induce cortical plasticity in the early stages. In addition, Bisio et al. (2017) indicated that 14 min of AO combined with ES training increased corticospinal excitability and induced cortical plasticity for at least 45 min after training. In agreement with the results of previous studies (Bisio et al. 2015a, b, 2017; Bonassi et al. 2017; Kaneko et al. 2014; Saito et al. 2013; Yamaguchi et al. 2012), the present findings suggest that the integration of MI-induced brain activation during AO and peripheral nerve ES-induced afferent input may be essential for efficiently inducing cortical plasticity. This evidence may support the application of AO–MI + ES training for enhancing plasticity and improving motor function in individuals after severe hemiparetic stroke (Okuyama et al. 2018). However, future studies are needed to confirm the effects of AO–MI + ES on the cortical plasticity and motor function in individuals with stroke.

In the present study, we found that the corticospinal excitability changes that were induced by AO–MI + ES and AO–MI alone depended on the imagery ability of the participants. It is known that kinaesthetic imagery ability correlates with the cortical excitability changes that occur during MI (Williams et al. 2012). Research has shown that muscle-specific and temporal modulations of the corticospinal pathway occur during kinaesthetic, but not visual, MI (Stinear et al. 2006). Hence, kinaesthetic imagery ability may be related to the changes in cortical excitability by both AO–MI + ES and AO–MI alone. However, a significant correlation between the cortical excitability changes and visual imagery ability was only found during the AO–MI + ES condition. The simplest explanation for this result is that cortical excitability changes might have occurred through the integration of visual information (by AO–MI) and sensory information (via ES) in the primary motor cortex (Corbet et al. 2018). Indeed, AO activates the frontal part of the mirror neuron system, which, in turn, activates the primary motor cortex through cortico-cortical connections (Calvo-Merino et al. 2006). Here, the activities induced by AO may have combined with those induced by MI, and, along with the afferent input provided by ES, may have enhanced the synaptic strength, leading to an enduring increase in corticospinal excitability (Bisio et al. 2015a, b, 2017; Corbet et al. 2018). Thus, visual imagery ability may be important for activating these circuits and inducing cortical plasticity during AO–MI + ES.

Previously, improvement in the motor function in the paretic upper extremity was reported after 4 weeks of MI training combined with EMG-triggered ES in patients with stroke (Hong et al. 2012). In another study, Kawakami et al. (2016) utilised a newer therapeutic concept, that is, a brain-machine interface triggered by MI combined with ES training, followed by hybrid assistive neuromuscular dynamic stimulation therapy (Fujiwara et al. 2009), to improve upper extremity motor function in patients with severe hemiparetic stroke who showed no EMG activity in the paretic arm. These prior findings, combined with the results of our study, provide evidence supporting that AO–MI + ES training can be effectively used in rehabilitation programs for patients with severe motor dysfunction after stroke.

Several limitations of this study should be noted. First, the sample size of the current study was small. Second, our study was conducted in healthy individuals. In the present study, the subjects were made to randomly participate in all the tasks to minimize the order effects of task on MEPs. However, we should have used a counterbalanced order to consider the issue more carefully. Therefore, future studies are needed to test the current approach in large samples comprising of patients with severe motor dysfunction after stroke.

In conclusion, our findings indicate that 10 min of AO–MI + ES can induce cortical plasticity, resulting in earlier changes in corticospinal excitability than with AO–MI or ES alone in healthy participants. Moreover, the corticospinal excitability changes that were induced by AO–MI + ES were correlated with the VMIQ-2 scores for visual and kinaesthetic imagery, suggesting that an individual's imagery ability may contribute to the induction of cortical plasticity following AO–MI + ES. However, we cannot provide the information on the duration of retention of the effects of AO–MI + ES on MEPs for the administered intervention timeframe. Further studies are required to clarify the efficacy and safety of applying AO–MI + ES in clinical settings for patients with severe motor dysfunction.

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Compliance with ethical standards

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare that they have no conflicts of interest.

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