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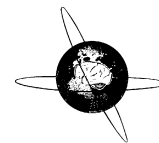
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Li, S., Stevens, J. A., & Rymer, W. Z. (2009). Interactions between imagined movement and the initiation of voluntary movement: a TMS study. *Clinical Neurophysiology*, 120(6), 1154-1160.

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Interactions between imagined movement and the initiation of voluntary movement: A TMS study

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See Editorial, pages 1031–1032

ARTICLE INFO

Article history:

Accepted 19 December 2008

Available online 27 February 2009

Keywords:

Motor imagery

Reaction time

Transcranial magnetic stimulation (TMS)

ABSTRACT

Objective: The purpose was to examine motor imagery-induced enhancement in corticospinal excitability during a reaction time (RT) task.

Methods: Nine young and healthy subjects performed an isometric finger flexion tasks in response to a visual imperative cue. In the pre-cue period, they were instructed to: (1) rest; (2) imagine flexing their fingers isometrically (ImFlex); or (3) imagine extending their fingers isometrically (ImExt). Surface EMGs from the finger flexors and extensors were monitored to ensure EMG silence before movement onset. Transcranial magnetic stimulation (TMS) was used to evaluate changes in motor-evoked potentials (MEP) in the finger flexor and extensor muscles during the response phase. TMS was delivered either with the imperative cue, or 120 ms before and after the imperative cue.

Results: RT was slower when they were imagining finger extension prior to the visual imperative cue. MEPs were significantly increased for the finger flexors during imagined finger flexion and for the finger extensors during imagined finger extension at both TMS delivery time points, reflecting movement specific enhancement in corticospinal excitability during motor imagery. When TMS was delivered 120 ms after the cue, finger flexor MEPs were further facilitated under the Rest and ImFlex conditions, but not under the ImExt condition, suggesting additive interactions between imagery-induced enhancement and early rise in corticospinal excitability during the initiation of a reaction time response.

Conclusions: Our results provide neurophysiological evidence mediating dynamic interactions between imagined movement and the initiation of voluntary movement.

Significance: Motor imagery can be integrated into a rehabilitation protocol to facilitate motor recovery.

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1. Introduction

Motor imagery (MI) is defined as imagining an actual movement without executing it. It is an active cognitive process in the first person during which the representation of a specific action is internally reproduced within working memory without any overt motor output, i.e., no discernible electromyographic (EMG) activities (Decety and Grezes, 1999; Jeannerod, 1995). However, motor imagery has measurable effects on the motor system and motor performance. A series of studies using transcranial magnetic

stimulation (TMS) provide evidence that motor imagery enhances focal cortical and corticospinal excitability (Decety, 1996; Facchini et al., 2002; Fadiga et al., 1999; Filippi et al., 2001; Fourkas et al., 2006; Jeannerod, 1995; Kasai et al., 1997; Li, 2007; Li et al., 2004b; Patuzzo et al., 2003; Sohn et al., 2003; Sparing et al., 2002; Stinear and Byblow, 2003; Yahagi and Kasai, 1999; Yahagi et al., 1996). Enhanced excitability is manifested by decreased motor threshold and facilitatory effects on motor-evoked potentials (MEPs) of the target muscles. We use the term “corticospinal excitability” to refer to the excitability of all the structures/pathways involved in the generation of responses to TMS, including both supraspinal and spinal mechanisms.

The MI-induced enhancement in corticospinal excitability has two distinct features, in addition to subthreshold enhancement. First, it is highly movement-specific to the target muscles of imag-

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ined movements. For example, although multiple finger representations are highly interconnected in the motor cortex (Schieber and Hibbard, 1993), individuals have the ability to imagine individual finger movements (Fadiga et al., 1999; Li, 2007; Li et al., 2004b; Rossini et al., 1999). These findings also support the view that the center and motor pathways used for imagined movement could be essentially the same as those used for voluntary movement, being facilitated at subthreshold levels during motor imagery (Li, 2007). Possibly due to involvement of the same structure and pathways, the second feature of motor imagery is that, similar to voluntary movements, the enhanced excitability can be dynamically modulated (Hashimoto and Rothwell, 1999; Stinear and Byblow, 2003). For example, Hashimoto and Rothwell (1999) reported phase-dependent modulation of MEPs during imagined wrist flexion and extension movements at 1 Hz, i.e., MEPs were larger in the wrist flexor muscles during the phase of imagined flexion than during extension, while the opposite was true for the extensor muscles. Similarly, the enhanced corticospinal excitability can also be voluntarily suppressed during imagined movement (Sohn et al., 2002, 2003).

Motor imagery, as an active cognitive process, has been reported to influence reaction time (Li et al., 2005). Reaction time (RT) measures the time interval between the onset of an imperative stimulus and the onset of movement. This period represents stimulus identification, central cognitive processing, and generation of an appropriate motor response (Hallett et al., 1991). Weiss (1965) found that variations in RT, secondary to set (preparatory interval), motivation, and age, predominately occurred in central cognitive processing. As such, any event that could complicate central cognitive processing of a RT task (Hanson and Loftus, 1978; Latash, 2000), would elongate RT. For example, to perform a simple visual RT task in context of motor imagery that increases the cognitive processing complexity significantly, resulting in an elongated RT (Li et al., 2005). The neurophysiological mechanism has not been investigated, however.

There is early rise in corticospinal excitability during a RT task, representing an increase from resting levels of activity, i.e., subthreshold enhancement of corticospinal excitability or early facilitation. Using transcranial electrical stimulation, Starr et al. (1988) showed that the MEP magnitude started to increase approximately 100 ms before the EMG onset of agonist muscle using a simple RT paradigm. A similar pattern of pre-EMG facilitation during RT tasks has been observed in a number of studies using TMS (Chen et al., 1998; Hoshiyama et al., 1996; Leocani et al., 2000; McMillan et al., 2004; Pascual-Leone et al., 1992). On the other hand, application of TMS during RT tasks influences execution of the movement. TMS lengthens the reaction time if applied close to the expected voluntary response, while it may shorten RT if applied early after the imperative stimulus (Leocani et al., 2000; Pascual-Leone et al., 1992; Ziemann et al., 1997).

The purpose was to quantify changes in corticospinal excitability that mediates the effect of motor imagery on reaction time. It was hypothesized that the movement-specific subthreshold-enhancement in corticospinal excitability during motor imagery could interact with a natural rise in corticospinal excitability during a reaction time task, resulting in dynamic modulation of corticospinal excitability during the pre-EMG facilitation period. To examine the interactions, we adopted an established MI-RT paradigm (Li et al., 2005). Delivery of TMS stimuli was preprogrammed before, on, or after the imperative visual cue, but before the EMG onset. MEPs measured from the flexor digitorum superficialis (FDS) and the extensor digitorum communis (EDC) were used to quantify changes in corticospinal excitability during RT-MI tasks. Reaction time tasks represent initiation of voluntary movement. Therefore, this study aimed to provide neurophysiological evidence mediating interactions between imagined movement (mo-

tor imagery) and initiation of voluntary movement. We hypothesized that MEPs of FDS and EDC depended on imagined movement (imagined flexion or extension) and on the time of TMS delivery (before, on or after), i.e., their interactions. Specifically, MEPs would be further increased when TMS was delivered during the early facilitation phase (i.e., after, not before or on the visual cue) for FDS only (not for EDC).

2. Methods

2.1. Subjects

Nine healthy individuals (1 male, 8 females) participated in this study. The mean age was 24.6 (± 0.9 SD) years with all reporting right hand dominance. All subjects gave informed consent according to the procedures approved by the Institutional Review Board at the University of Montana. Inclusion criteria were healthy adults. Exclusion criteria were adults with a history of a neurological disorder or musculoskeletal injury of the upper extremities, or a history of a brain injury or seizure, or any intracranial metal objects, a pacemaker, or other implanted devices.

In this study, subjects were instructed to perform a squeezing reaction time task with and without a background imagined movement. The delivery of TMS stimuli was preprogrammed at 120 ms before (TMS₋₁₂₀), on (TMS₀), or 120 ms after (TMS₁₂₀) the imperative visual cue. Specific instructions, sufficient practice trials and on-line feedback were used to ensure EMG silence during motor imagery or at rest. Off-line analyses of background EMG activities showed no significant difference among different conditions for both FDS and EDC muscles, respectively, thus confirming EMG silence.

2.2. Experimental set-up

In a darkened room, a desktop computer was positioned on the testing table about 1.2 m in front of the subjects. Subjects were seated comfortably in front an experimental table. The right upper shoulder was at approximately 45° of abduction in the frontal plane and 45° of flexion in the sagittal plane, elbow joints at approximately 135° of flexion. The left forearm and hand rested on the testing table at most of time at the same height as the right forearm. The right hand rested in a “grasping” configuration in contact with a customized handle, as used in a previous study (Li et al., 2005). The fingers were taped onto the handle using 3M adhesive tape such that the fingers were unmovable during imagined finger flexion and extension.

2.2.1. Transcranial magnetic stimulation (TMS)

The method and procedures of application of TMS was the same as described in previous studies (Danion et al., 2003; Li, 2007; Li et al., 2004b). Focal TMS was performed with a figure-of-8-shaped stimulation coil (mean diameter of each wing 35 mm) connected to a Magstim 200² monophasic transcranial magnetic stimulator with the maximal magnetic field strength of 2.2 T (Magstim Corp., UK). The intersection of the coils was placed tangentially to the scalp, approximately positioned 2 cm to the left of the vertex (Cz), with the handle pointing backward and laterally at a 45° angle away from the midline. In this way, the current induced in the neural tissue was directed approximately perpendicular to the line of the central sulcus in a direction parallel to the mid-line between the two coils and therefore optimal for activating the corticospinal pathways transsynaptically (Brasil-Neto et al., 1992). In search of an optimal position for the finger flexors of the right hand, the stimulus intensity was set at 60% of the stimulator output and the coil was moved over the scalp in steps of 1 cm. The optimal position was defined by eliciting the largest MEP in the finger flexors

that was stable in three consecutive trials. Keeping the coil at the optimal location, the stimulation intensity was slowly decreased until the resting motor threshold (MT) was found. The MT was defined as the lowest stimulus capable of evoking at least 5 of 10 discernable motor evoked potentials (MEPs) with the amplitude of at least 50 μV when subjects were at rest. The stimulation intensity was the same for the rest and motor imagery conditions, i.e., 150% of the resting MT. Delivery of magnetic stimulation was programmed with respect to the visual go-signal onset (see below).

2.2.2. Motor imagery

Subjects were instructed to perform two different motor imagery tasks – imagined finger flexion (ImFlex) and imagined finger extension (ImExt). During ImFlex tasks, subjects were instructed to imagine pressing four fingers of their right hand (i.e., from the first person) against the handle isometrically as hard as possible after a verbal command (standard command “relax, ready, go” was given prior to the beginning of a trial) and sustain this condition after a reaction response (squeezing the hand) to the visual go-signal. Furthermore, subjects were instructed to close mouths and to keep all muscles relaxed as in the rest condition.

For ImExt tasks, all instructions and procedures were the same as for ImFlex tasks except that subjects were instructed to imagine exerting maximal isometric finger extension force with four fingers of their right hand while resting in a “grasping” configuration in contact with the handle. Since the fingers were taped to the handle, ImExt and ImFlex tasks were viewed as symmetrical tasks.

At rest, subjects were instructed to close their mouths and to keep all muscles relaxed. Furthermore, subjects were also instructed not to imagine or visualize any movement (e.g., fingertip force production), or to be engaged in cognitive activities (e.g., counting, worrying) to ensure a resting mental state.

To assist subjects perform motor imagery tasks (Li et al., 2005), a photo ($8 \times 8 \text{ cm}^2$) of a hand in either grasping or opening configuration, mimicking the real grasping or finger extension actions, was positioned to the right of the LED square on the computer screen. The subjects were instructed to visualize his/her own hand on the computer screen and to perform imagined finger flexion or extension while staring at the photo. According to the feedback from subjects in the pilot study, both the LED square and the photo were within their field of vision; they had no difficulty performing imagery tasks and responding to the go-signal during reaction time tasks.

2.2.3. Simple RT tasks

A LED square ($8 \times 8 \text{ cm}^2$) centered on the computer screen was randomly turned from “grey” to “blue” and maintained “blue” until the end of trial. Each trial lasted 10 s. The onset of visual go-signal was preprogrammed from 4 to 7 s with an interval of 1 ms. Subjects were asked to respond to the visual go-signal as quickly as possible by actually squeezing the handle. To minimize the effect of TMS click noise on reaction time, subjects wore shooting ear muffs throughout the experiment, including trials without TMS applications.

2.3. Experimental procedures

Two sets of experimental tasks were performed, RT during motor imagery with or without TMS applications. RT tasks without TMS applications were performed first to confirm the previous findings (Li et al., 2005): (1) ImFlex, (2) ImExt; and (3) Rest. Conditions were randomized. Each condition consisted of 8 trials.

To examine dynamic modulation of MI-induced corticospinal excitability, the following RT tasks with TMS applications were performed: (1) ImFlex₋₁₂₀; (2) ImFlex₀; (3) ImFlex₁₂₀; (4) ImExt₋₁₂₀; (5) ImExt₀; (6) ImExt₁₂₀; (7) Rest₋₁₂₀; (8) Rest₀; and (9) Rest₁₂₀.

Numbers refer to the moment when TMS stimuli were delivered: 120 ms before (TMS₋₁₂₀), on (TMS₀), or at 120 ms after (TMS₁₂₀) the visual go-signal. For example, ImFlex₁₂₀ indicates a task that subjects were instructed to react to the go-signal while performing the ImFlex task; the go-signal was randomly turned on between 4 and 7 s while TMS was preprogrammed at 120 ms after the go-signal. These conditions were randomized. Each condition had 8 trials.

Each subject had a familiarization session. This session took approximately 15 min to ensure EMG silence during RT tasks, and RT-MI tasks. EMG silence was defined as the absence of any background activity at the sensitivity of 25 μV per division (Facchini et al., 2002; Li, 2007; Li et al., 2004b). The employed high resolution of EMG sensing system was capable of detecting deviation of EMG signals from the background levels due to the slightest movement of individual fingers. Trials were discarded if EMG activities occurred. These trials were repeated in order to maintain the same number of trials for each condition. A 2-min break was allowed after every three conditions.

2.4. Recordings

A desktop computer was used for data acquisition and processing. Differential surface EMG electrodes (DelSys Inc., Boston, MA) were placed over the muscle bellies of the finger flexors (FDS) and finger extensors (EDC) of the right arm to obtain EMG signals. The EMG signals were amplified, digitized and high-pass filtered at 10 Hz and low pass filtered at 500 Hz. The signals were sampled at 1000 Hz by a 16-bit A/D board using customized LabView software (National Instrument, Austin, TX). The digitized FDS and EDC EMG signals were set at a high gain (25 μV per division) for on-line monitoring. All EMG signals were saved for off-line analysis.

2.5. Data analysis

The methods for measuring magnitude and latency of MEPs were the same as previously described (Li, 2007; Li et al., 2004b). Because changes in motor threshold and latency of MEP during motor imagery have been well documented in the literature (Facchini et al., 2002; Fadiga et al., 1999; Li et al., 2004a), these parameters were recorded, but not the main dependent variables in this study.

Briefly, from the rectified, unfiltered EMG signal, the background EMG (EMG_{BC}) was defined as the mean EMG calculated from -100 ms to the visual signal onset (TMS₀ and TMS₁₂₀), or to the moment of TMS application when TMS was delivered prior to the visual signal (TMS₋₁₂₀). The MEP latency was computed as the interval between the TMS delivery and the time when it took the baseline EMG to increase by 2 SDs. The MEP size was defined as the difference between the peak EMG in the rectified signal (within 50 ms after TMS application) and EMG_{BC} (Danion et al., 2003). The MEP size was normalized to the maximal MEP value obtained from a subject. The maximal MEP was usually in a trial during ImFlex at TMS₁₂₀ for FDS and in a trial during ImExt at TMS₋₁₂₀ for EDC. EMG_{BC}, latency and MEPs were calculated for both FDS and EDC, respectively.

Reaction time was measured from the FDS EMG signal (Li et al., 2005). RT was defined as the time interval between the go-signal onset (t_0) and the FDS EMG onset (t_{EMG}). t_{EMG} was computed as the moment when it took the baseline EMG to increase by 2 standard deviations (SD).

2.6. Statistics

Descriptive and repeat-measures ANOVAs were used. We first compared the effect of TMS on reaction time to assess the potential intersensory facilitation effect. Two-way ANOVAs were used with factors TMS (2 levels, TMS = 0 ms and NoTMS), and IMAGERY (3

levels, ImFlex, ImExt, and Rest). The effect of TMS delivery time on RT was subsequently examined with factors TIME (3 levels, TMS₋₁₂₀, TMS₀, and TMS₁₂₀) and IMAGERY. Three-way ANOVAs were used to compare background EMG activities for both FDS and EDC under different conditions to confirm EMG silence. Factors were MUSCLE (2 levels, FDS and EDC), IMAGERY, and CONDITION (4 levels, TMS₋₁₂₀, TMS₀, TMS₁₂₀, and NoTMS). To examine interactions between motor imagery and reaction, as reflected by changes in the normalized MEP, two-way ANOVAs were used with factors IMAGERY and TIME for FDS and EDC, respectively. Wherever justified, Tukey post-hoc analyses were used to locate the significance. The level of significance was set at $p \leq 0.05$.

3. Results

3.1. Effects on RT

We found that mean RT, the interval between the go-signal and the FDS EMG onset, was influenced by both motor imagery and TMS applications, as shown in Fig. 1 (comparing TMS₀ and NoTMS columns). A two-way ANOVA showed main effects of IMAGERY ($F_{[2,16]} = 8.17, p = 0.004$), TMS ($F_{[1,8]} = 15.6, p = 0.004$), and a significant interaction IMAGERY \times TMS ($F_{[2,16]} = 7.04, p = 0.006$). According to post-hoc tests, RT was significantly greater in ImExt (333.6 ms) than in ImFlex (276.6 ms) and Rest (266.4 ms) ($p < 0.008$) when there were no TMS applications (Fig. 1, NoTMS, asterisk). No significant difference in RT was found between Rest and ImFlex. TMS applications significantly decreased RT from 292.2 ms (NoTMS) to 233.8 ms (TMS₀) ($p = 0.004$). The significant reduction in RT, however, was found for both ImFlex (276.6 ms vs. 224.7 ms, $p < 0.018$) and ImExt (333.6 ms vs. 235.6 ms, $p < 0.001$), but not for Rest (266.4 ms vs. 241.0 ms, $p = 0.475$). RT showed no significant differences among conditions (ImFlex, ImExt, and Rest) with TMS₀.

Timing of TMS delivery changed RT (Figs. 1 and 2). As depicted in typical trials (Fig. 2), RT was influenced by the TMS delivery time. A two-way ANOVA showed a main effect of TIME ($F_{[2,16]} = 33.19, p < 0.001$). Post-hoc tests revealed that RT at TMS₁₂₀ (328.6 ms) was significantly greater than RT at TMS₋₁₂₀ (193.7 ms) and TMS₀ (233.8 ms), respectively ($p < 0.001$), while no difference was found between the latter two. At each TMS delivery time point (TMS₋₁₂₀, TMS₀, and TMS₁₂₀), RT was not different among different imagery conditions (Fig. 1).

3.2. Effects on motor-evoked potentials (MEPs)

TMS was delivered prior to, on, or after the go-signal in MI-RT tasks. The MEP magnitude, normalized to the obtained largest

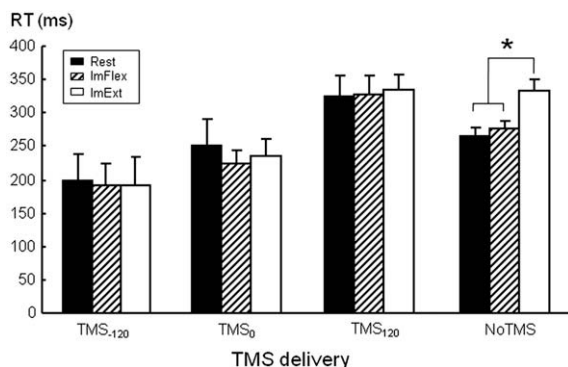


Fig. 1. The averaged reaction time (RT) with standard error bars. TMS₋₁₂₀, TMS₀, TMS₁₂₀ indicates TMS delivery at 120 ms prior to, on, and 120 ms after the visual go signal. ImFlex: imagined finger flexion; ImExt: imagined finger extension. Asterisk indicates statistical significance.

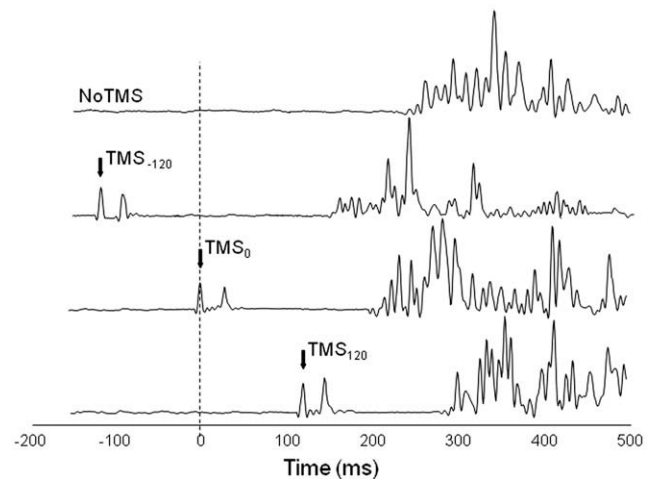


Fig. 2. The effect of TMS delivery on reaction time at rest. The rectified, filtered FDS EMG signals from typical trials of the same subjects are plotted. Arrows denotes the delivery of TMS, vertical line: the go-signal; numbers: timing of TMS with respect to the visual go signal.

value for a subject, was dependent upon motor imagery and TMS delivery for both FDS and EDC muscles (Fig. 3). For normalized FDS MEP magnitudes (Fig. 3A), a two-way ANOVA revealed significant effects of IMAGERY ($F_{[2,16]} = 4.66, p = 0.025$) and TIME ($F_{[2,16]} = 33.95, p < 0.001$), and a significant interaction IMAGERY \times TIME ($F_{[4,32]} = 34.42, p < 0.001$). Post-hoc tests revealed that, there were no difference between ImExt and Rest conditions at TMS₋₁₂₀ or TMS₀; the FDS MEP remained unchanged during ImExt across different TMS delivery times (Fig. 3A, dotted line); the FDS MEP was greater at Rest than during ImExt at TMS₁₂₀ ($p < 0.001$). Furthermore, the FDS MEP was significantly greater during ImFlex than during ImExt and Rest across all TMS delivery time points

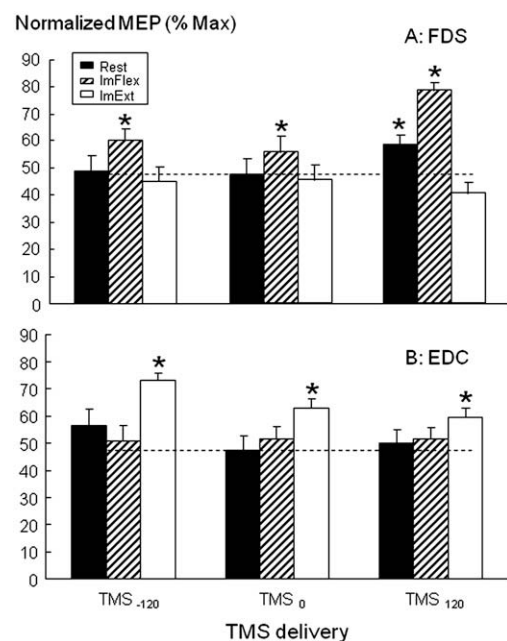


Fig. 3. The motor-evoked potentials (MEP) (A: FDS, B: EDC). MEPs were normalized to individual maximal values. TMS₋₁₂₀, TMS₀, TMS₁₂₀ indicates TMS delivery at 120 ms prior to, on, and 120 ms after the visual go signal. ImFlex: imagined finger flexion; ImExt: imagined finger extension. Standard error bars are shown. Asterisk indicates statistical significance. Dotted line indicates the baseline FDS and EDC MEP, respectively, at rest at TMS₀.

($p < 0.001$). Similarly, the normalized EDC MEP magnitudes (Fig. 3B) were also dependent on TMS delivery time ($F_{[2,16]} = 3.65$, $p = 0.049$) and motor imagery (IMAGERY, $F_{[2,16]} = 8.03$, $p = 0.004$). The EDC MEP was greater during ImExt than during ImFlex and at Rest at all TMS delivery time points (i.e., above the dotted line in Fig. 3B), while no difference between ImFlex and Rest were found. The EDC MEP decreased from TMS₋₁₂₀ to TMS₁₂₀ ($p = 0.052$), while the EDC MEP at 0 ms was not different from these two.

4. Discussion

In this study, subjects reacted to an imperative visual cue (a screen light) by squeezing a handle in the context of imagined movement of finger flexion or finger extension or at rest. Motor evoked potentials (MEPs) from the finger flexors (FDS) and extensors (EDC) in response to preprogrammed TMS stimuli were recorded to quantify changes in corticospinal excitability during the combined motor imagery-reaction time tasks. The main findings were: (1) MEPs were significantly increased for the finger flexors during imagined finger flexion, for the finger extensors during imagined finger extension at all TMS delivery time points; (2) When TMS was delivered 120 ms after the imperative visual cue, the FDS MEPs were further facilitated under the Rest and ImFlex conditions, but not under the ImExt condition; (3) RT was slower when they were imagining finger extension prior to the visual cue; and (4) RT was elongated when TMS was delivered at 120 ms after the cue, but remained unchanged at other points.

4.1. Effect on corticospinal excitability

In previous reports, corticospinal excitability of the prime mover, indicated by MEPs, increased gradually over the 80–120 ms before EMG onset during reaction time tasks (Chen et al., 1998; Hoshiyama et al., 1996; Leocani et al., 2000; McMillan et al., 2004; Pascual-Leone et al., 1992; Starr et al., 1988). MEP facilitation has also been reported as early as 160–200 ms preceding EMG onset (Leocani et al., 2000). In our current study, the averaged RT was 266 ms at rest without TMS application. Given the fact that TMS delivered close to the EMG onset could lengthen reaction time (Day et al., 1989), the measured increase in the FDS MEP at TMS₁₂₀ during ImFlex tasks could indicate early facilitation at about 146 ms (266–120 ms) before the FDS EMG onset. Our observation of early rise in corticospinal excitability during RT tasks is generally in agreement with these previous reports.

We also observed that MEPs were greater for FDS during imagined finger flexion (ImFlex) and for EDC during imagined finger extension (ImExt) at all TMS delivery points (Fig. 3). These results confirmed earlier reports of subthreshold enhancement in corticospinal excitability during motor imagery (Fadiga et al., 1999; Li, 2007; Li et al., 2004a,b; Rossini et al., 1999). Furthermore, the contrasting results of an increased FDS MEP during ImFlex and an unchanged FDS MEP during ImExt (Fig. 3A) indicated that corticospinal excitability for the finger flexors was specifically enhanced during ImFlex, but not during ImExt. An opposite pattern of results was observed for the EDC MEP (Fig. 3B). These results further supported the view of movement-specific subthreshold enhancement of the target muscles during motor imagery (Li, 2007).

Of particular interest, our results provided evidence for interactions between MI-induced enhancement and early rise in corticospinal excitability during RT tasks (Fig. 3). As mentioned earlier, an increased FDS MEP at TMS₁₂₀ at rest reflected early facilitation during RT tasks. Further increase in the FDS MEP during ImFlex at TMS₁₂₀ could be viewed as the additive interaction between movement-specific enhancement effects of MI and the natural rise

of corticospinal excitability in reaction time tasks. The MI-RT interaction was further supported by the result of unchanged FDS MEP at TMS₁₂₀ during ImExt tasks. RT-induced early facilitation for the finger flexors at TMS₁₂₀ was likely to be balanced by MI-induced movement-specific enhancement in the finger extensor excitability during ImExt tasks via reciprocal inhibition mechanisms, resulting in an unchanged FDS MEP (Fig. 3). Alternatively, this unchanged FDS MEP may be due to a longer interval (334 – 120 = 214 ms) between the expected EMG onset during ImExt (334 ms) and TMS delivery (120 ms). As such early facilitation may have not occurred yet. However, smaller EDC MEP at TMS₁₂₀ than at TMS₋₁₂₀ may suggest that the finger extensor excitability have been balanced by early activation, even with no change in FDS MEP.

The dynamic MI-RT interactions are illustrated graphically in Fig. 4. At rest, corticospinal excitability for the finger flexors gradually rises from a resting potential before it reaches the motor threshold during RT tasks (i.e., early facilitation, solid-line curve). Due to movement-specific subthreshold enhancement in corticospinal excitability during motor imagery, the early facilitation curve is elevated during ImFlex, showing additive effects (thick dashed-line curve). In contrast, the early facilitation is balanced by MI-induced enhancement in the finger extensors during ImExt, resulting in a right shift of the curve (thin, dashed-line curve). This model helps understand conceptually underlying mechanisms that mediate the effect of MI-RT interactions on RT in the next section.

4.2. Effect on RT

In the present study, RT was significantly elongated during ImExt, but remained unchanged during ImFlex (when compared to RT at rest without TMS application). These results confirmed our previous findings (Li et al., 2005). Quantification of changes in the FDS and EDC MEPs in the present study (Figs. 3 and 4) provided evidence that the effect of motor imagery on RT was mediated by concomitant changes in corticospinal excitability, as was proposed in our earlier study (Li et al., 2005).

Since motor imagery is an active cognitive process (Decety and Grezes, 1999), it conceivably increases task complexity. Analogous to choice RT tasks, motor imagery imposes a general inhibitory effect on the central cognitive processing, resulting in an elongated RT. On the other hand, motor imagery induces movement-specific subthreshold-enhancement in corticospinal excitability of the prime mover (Facchini et al., 2002; Fadiga et al., 1999; Li, 2007; Li et al., 2004a,b; Rossini et al., 1999; Stinear and Byblow, 2004). During squeezing RT tasks, the overall inhibitory effect may be balanced by MI-induced enhancement in the finger flexors during ImFlex. Therefore, no change in RT was observed. In contrast,

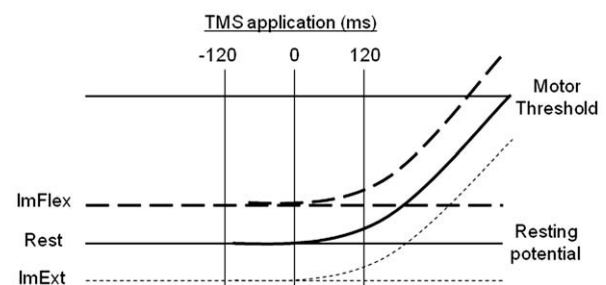


Fig. 4. Conceptual illustration of motor imagery-reaction time dynamic interactions. During squeezing reaction time tasks, there is a natural facilitation course of finger flexor corticospinal excitability (solid curve line). Motor imagery of agonist (ImFlex) brings resting potentials of finger flexors closer to motor threshold (i.e., subthreshold enhancement), thus showing additive effects (thick dotted line); while motor imagery of antagonist (ImExt) leads to inhibitory effects on resting potentials of finger flexors (thin dotted line).

MI-induced subthreshold enhancement in corticospinal excitability for the finger extensors during ImExt could impose further inhibitory effects on squeezing reaction time tasks, possibly via reciprocal inhibitory mechanisms, thus leading to an elongated RT.

Other factors could potentially influence RT in this study, however. These factors include TMS application, auditory cues, and action observation. According to previous reports, TMS application dramatically influences RT. The effect of TMS on RT depends on timing (relative to the go-signal) (Pascual-Leone et al., 1992; Sawaki et al., 1999; Ziemann et al., 1997), site (Schluter et al., 1998), and intensity (Pascual-Leone et al., 1995; Ziemann et al., 1997) of TMS application. For example, TMS applied to the contralateral motor cortex lengthens RT. The lengthening is longer with higher stimulus intensity and is most evident when the TMS is delivered just before the expected time of movement (Ziemann et al., 1997). Such delay in RT is reported up to 150 ms (Day et al., 1989). In this study, TMS delivered at 120 ms after the visual cue delayed RT approximately 95 ms (323 ms at TMS₁₂₀ and 238 ms at TMS₀). Early TMS delivery at –120 ms, however, slightly facilitated reaction time tasks (193 ms at TMS₋₁₂₀). It may be possible that the click noise associated with TMS serves as an auditory cue to trigger reaction time responses, via inter-sensory facilitation (Terao et al., 1997), although it could have been minimized by wearing shooting muffs.

Interestingly, at each TMS delivery time point, we observed no effect of motor imagery on RT when TMS was applied (Fig. 1). It has been reported that TMS can transiently interrupt the process of movement in the motor cortex without affecting the pattern of the agonist and antagonist EMG bursts (Day et al., 1989; Ziemann et al., 1997). One possible explanation could be that the MI-induced enhancement in corticospinal excitability subsequent to an active cognitive process of motor imagery is interrupted by TMS, resulting in no change in RT across different motor imagery status. Another possibility is that the TMS click noise could serve as an auditory cue to trigger reaction time movements.

Furthermore, subjects were instructed to perform motor imagery tasks while they were looking at pictures (visual aid) on the computer screen. In this experimental setting, it was hard to distinguish performing motor imagery from action observation. Although action observation has been reported to produce similar levels of corticospinal facilitation (Clark et al., 2004), motor imagery involves additional task-specific and modal processing supraspinal areas (Munzert et al., 2008). As such, this limitation in experimental design could increase variations of RT.

5. Concluding remarks

In addition to providing further evidence for movement-specific subthreshold enhancement in corticospinal excitability during motor imagery and early rise in corticospinal excitability during reaction time tasks, we clearly demonstrate interactions between changes in corticospinal excitability induced by motor imagery and during reaction time tasks, resulting in dynamic modulation of corticospinal excitability. As a consequence of active cognitive process, MI-induced corticospinal changes have been reported to be volitionally manipulated, e.g., volitionally suppressed (Sohn et al., 2002, 2003), phase-dependent changes during imagined cyclic wrist movement (Hashimoto and Rothwell, 1999; Stinear and Byblow, 2003). Our results extend these findings that MI-induced corticospinal excitability changes can interact with early facilitation in corticospinal excitability during voluntary movements (reaction time tasks). As such, our results strongly support the view that motor imagery effects on motor performance can be consolidated with minimal physical practice (Pascual-Leone et al., 1995), and that motor imagery can potentially be utilized for improving motor recovery in stroke survivors (Lotze and Cohen,

2006; Sharma et al., 2006; Stevens and Stoykov, 2003), possibly via interactions between imagined movement and voluntary movement.

Acknowledgments

The authors thank Woo-Hyung Park, Ph.D. for his technical support, and Megan Longenecker, Courtney O'Rear, ZhohnAnn Piva, Ryan Strecker for their assistance in data acquisition. This study was supported in part by NIH Grants (R15NS053442 and R01NS060774).

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