

Repetitive Transcranial Magnetic Stimulation to the Primary Motor Cortex Interferes with Motor Learning by Observing

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Abstract

■ Neural representations of novel motor skills can be acquired through visual observation. We used repetitive transcranial magnetic stimulation (rTMS) to test the idea that this “motor learning by observing” is based on engagement of neural processes for learning in the primary motor cortex (M1). Human subjects who observed another person learning to reach in a novel force environment imposed by a robot arm performed better when later tested in the same environment than subjects who observed movements in a dif-

ferent environment. rTMS applied to M1 after observation reduced the beneficial effect of observing congruent forces, and eliminated the detrimental effect of observing incongruent forces. Stimulation of a control site in the frontal cortex had no effect on reaching. Our findings represent the first direct evidence that neural representations of motor skills in M1, a cortical region whose role has been firmly established for active motor learning, also underlie motor learning by observing. ■

INTRODUCTION

Humans learn how to behave by observing and imitating the actions of others. There are different levels at which action observation can influence action selection and performance. Consider a pair of golfers. On one level, watching a partner’s successful shot may motivate the observer to attempt the same action (Heyes, 1994; Heyes & Dawson, 1990; Bandura, 1986), or it may influence the observer’s choice of target location (Bandura & Jeffrey, 1973). On a perceptual level, by observing a partner’s swing, the observer can garner visual information about the angle of the club at the top of the swing and acoustic information about the “swoosh” of the club head at the bottom of the swing. This perceptual information may inform the observer about what outcomes need to be achieved during performance (Frey & Gerry, 2006; Lozano, Hard, & Tversky, 2006; Heyes & Foster, 2002; Carroll & Bandura, 1987, 1990), but it does not necessarily inform the observer about *how* to achieve these outcomes at a motor level. Given that observing the actions of others engages neural mechanisms that are involved in performing those actions (Shmuelof & Zohary, 2005, 2006; Fogassi et al., 2005; Patuzzo, Fiaschi, & Manganotti, 2003; Watkins, Strafella, & Paus, 2003; Gallese, Fogassi, Fadiga, & Rizzolatti, 2002; Baldissera, Cavallari, Craighero, & Fadiga, 2001; Buccino et al., 2001; Gangitano, Mottaghy, & Pascual-Leone, 2001;

Strafella & Paus, 2000; Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Rizzolatti, Fadiga, Gallese, & Fogassi, 1996; Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995; Di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992), here we consider the possibility that observation engages learning mechanisms in the motor system that allow the observer to learn *how* to produce an appropriate, coordinated action at a motor level—for example, how to generate appropriate patterns of muscle forces.

The intriguing possibility that action observation leads to learning at the level of the motor system is supported by the results of Mattar and Gribble (2005). Participants observed naïve actors learning to reach in a clockwise, velocity-dependent force field (CWFF) or a counterclockwise force field (CCWFF) imposed on the limb by a robot arm. Participants who watched another person learning to reach in the CWFF performed better when later exposed to the CWFF in comparison to participants who did not observe. In contrast, participants who observed another person learning to reach in the CCWFF performed worse. As the ability to compensate for a force-field perturbation is a direct reflection of the extent to which the motor system has learned to predict the perturbing forces (Flanagan, Vetter, Johansson, & Wolpert, 2003; Haruno, Wolpert, & Kawato, 2001; Flanagan & Beltzner, 2000; Shadmehr & Holcomb, 1997; Shadmehr & Mussa-Ivaldi, 1994), Mattar and Gribble proposed that observers acquired neural representations of the novel force fields through implicit engagement of learning mechanisms in the motor system.

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Here we directly tested the hypothesis that action observation engages learning mechanisms in the primary motor cortex (M1) by applying repetitive transcranial magnetic stimulation (rTMS) to M1 after force-field (FF) observation, and by studying the effects on subsequent retention of observation-related motor learning. rTMS has been used to study the functional role of brain areas by imposing what is sometimes referred to as a temporary “virtual lesion” to a specific cortical region (Pascual-Leone, Walsh, & Rothwell, 2000; Jahanshahi & Rothwell, 1999). More specifically, it has been demonstrated that rTMS selectively reduces the excitability of the motor cortex for roughly 15 min following treatment (Chen et al., 1997). If observation engages learning mechanisms in M1, rTMS should interfere both with the beneficial effect of observing the congruent FF information and with the detrimental effect of observing incongruent FF information. Finally, to rule out nonspecific effects of cortical stimulation, we compared the effectiveness of rTMS applied to M1 to stimulation of a control site in the superior frontal lobule (SFL).

METHODS

Participants

Fifty-four participants completed the study. All participants reported being right-handed, with normal or corrected-to-normal vision, and no history of any neurological or musculoskeletal disorder. All gave written informed consent before participation. No participant had previous experience with the robotic manipulandum. Participants receiving TMS were screened for standard conditions for exclusion associated with TMS and magnetic resonance imaging (MRI; Wasserman, 2002). The UWO Research Ethics Board approved all procedures.

Twelve participants were assigned to each of the three non-TMS treatment groups and six participants were assigned to each of the three TMS cortical treatment groups. Each participant experienced only one experimental condition.

Motor Learning Task

Each participant was seated at a table at chest height. A custom-made air-sled supported the participant’s right arm against gravity and allowed the arm and hand to move over the surface of the horizontal table with little friction. The participant grasped the handle of an InMotion2 robotic manipulandum (InMotion Technologies, Cambridge, MA) and used the robot to reach to visually displayed targets.

Computer-generated displays were projected by an LED projector (Sony VPL-CS1) onto an angled mirror suspended above the workspace. The angled mirror reflected the display onto a horizontal back-projection

screen (105 cm × 60 cm) and horizontal semi-silvered mirror (107 cm × 75 cm) that were supported above the table surface. The robotic arm was positioned below the surface of the mirror and moved parallel to the table surface. This arrangement gave participants the impression that the visual items were displayed in the same horizontal plane in which the movements were performed (see Figure 1).

Reaching movements were made from a central start location toward one of eight peripheral targets positioned at a constant radial distance (10 cm) at 45° intervals (Figure 1, inset). The position of the hand was represented in real time by a cursor on a screen directly in front of the participant. When the participant used the manipulandum to place the cursor in the central start location, a peripheral target appeared. The presentation of targets was pseudorandomized over a series of eight movements. This eight-target cycle was repeated 12 times per block, for a total of 96 movements per block.

The robotic manipulandum was programmed to produce forces that acted at the hand, proportional to the velocity of movement. These forces acted in a clockwise (CWFF) direction defined by the following equation:

$$\begin{bmatrix} F_x \\ F_y \end{bmatrix} = \begin{bmatrix} 0 & k \\ -k & 0 \end{bmatrix} \begin{bmatrix} xY' \\ yY' \end{bmatrix} \quad (1)$$

where F_x and F_y are forces generated by the manipulandum in the left/right and forward/backward directions, respectively, xY' and yY' denote hand velocities, and $k = 15$ Ns/m. In some parts of the experiment, the manipulandum produced no forces (a null field, $k = 0$).

Robot handle positions (x, y) were sampled at 500 Hz and stored on a digital computer. We measured maximum movement curvature, the maximum deviation of the hand path from the straight line connecting the spatial location of start of the movement with the location of

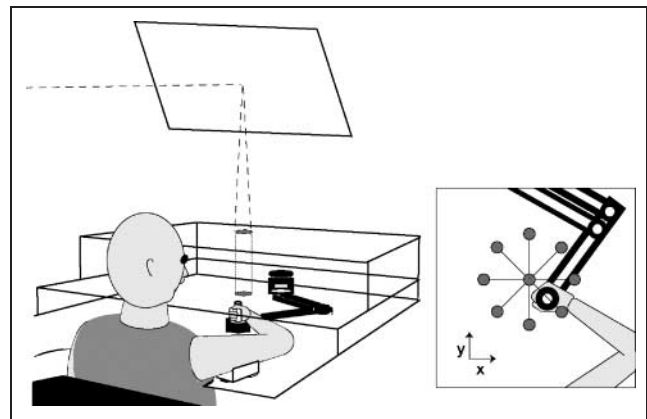


Figure 1. Experimental setup. Participants grasped the handle of the robotic manipulandum and moved it to guide a visible cursor from a central start position to a peripheral target (shown in inset).

the end of the movement. Positive curvature values indicated a deviation in the CW direction and negative values indicated a deviation in the CCW direction. We also measured movement time, where movement initiation was defined as the time at which tangential velocity first exceeded 0.05 msec^{-1} and movement end was defined as the first time after peak velocity that tangential velocity fell below 0.05 msec^{-1} . Peak tangential velocity was also recorded.

Video Recordings for Observation

The video recordings have been described in detail elsewhere (Mattar & Gribble, 2005). Briefly, participants observed video recordings of healthy naïve undergraduates making targeted reaching movements as the robotic manipulandum applied either a clockwise (CWFF) or counterclockwise (CCWFF) perturbing force field to the actor's hand. The videos provided participants with a top-down view of the head and shoulders of the actor, superimposed by a translucent image of the visual targets and the cursor showing the position of the actor's hand. Each recording was approximately 6 min in duration and showed a series of 96 movements. Participants viewed the appropriate video twice.

Participants (observers) were instructed to watch the videos while keeping their arm still. A number was displayed in the upper left corner of the display that corresponded to the actor's trial number. To ensure that observers were attending to the video, we instructed subjects to verbally report trial numbers on which the actor made a movement timing error (indicated by the actor's target turning red or green).

Transcranial Magnetic Stimulation

All participants receiving TMS underwent a high-resolution (1 mm^2 voxels) T1-weighted, full head anatomical MRI scan in a 4-Tesla Siemens-Varian scanner. The MR images were used to guide the positioning of the TMS coil over the scalp during single pulse and rTMS. A three-dimensional reconstruction of each participant's brain was coregistered with his or her head position and volume using Brainsight software (Rogue Research, Montreal, Canada) and a Polaris infrared motion tracking device (Northern Digital, Waterloo, Canada) using nine landmarks visible both on the scan and on the head (see Cothros, Kohler, Dickie, Mirsattari, & Gribble, 2006 for further detail).

A standard step procedure (Muellbacher et al., 2002) was used to determine participants' individual thresholds for eliciting a resting motor evoked potential (MEP) in the right first dorsal interosseous muscle from single-pulse TMS applied to the contralateral (left) primary motor cortex (M1). Two surface electromyography (EMG) electrodes (Grass Instruments, Astromed) were placed over this muscle, and over the right extensor carpi radialis, the right long head of biceps brachii, and the right

middle deltoid muscles. MEPs were viewed on a software oscilloscope (Grass Instruments, Astromed). After finding the resting motor threshold (RMT) for the first dorsal interosseous muscle, further single pulses were delivered at 110% RMT to target the M1 representation of the long head of biceps brachii (an elbow flexor) and middle deltoid (a shoulder abductor and flexor). To improve the likelihood that muscles involved in horizontal planar reaching would be targeted by rTMS, pulses were applied to a location between elbow and shoulder muscle representations. We also applied rTMS to a control site that is not associated with force-field adaptation, the left superior frontal gyrus. We determined the location of this site by first locating and placing a virtual marker over the lateral-most position on the left insula. We then viewed the lateral aspect of the left hemisphere and followed an imaginary line that ran perpendicular and superior to the Sylvian fissure from this marked insular position to the SFL (see Cothros et al., 2006).

TMS pulses were delivered using an air-cooled figure-of-eight coil, controlled by a biphasic rapid rate stimulator (Magstim). To apply both single and rTMS pulses, the participant's head was stabilized in a chin rest. Brainsight software was used to visualize a cursor on the computer screen that represented the estimated real-time position of the vertex of the TMS coil over the cortex as the coil was positioned over the participant's scalp. The coil was oriented so that the direction of the induced current in cortex flowed in a postero-anterior direction. The TMS coil was held in place on the participants' scalp by a multilink adjustable clamp (Manfrotto). The duration of the rTMS train was 15 min, at a frequency of 1 Hz, and at an intensity of 110% RMT.

Procedure

The design of the experiment is presented in Table 1. All participants initially performed the reaching task (92 trials) in a null (zero force) field. Then depending on the condition to which they were assigned, they experienced a 30-min delay, or they watched the CCWFF or CWFF video. Participants were instructed to watch the videos and report the trial number on which they saw the actor make an error. The videos were played twice in succession. Then depending on the condition to which they were assigned, participants received either a 15-min treatment of rTMS or they experienced a 20-min delay. Finally, all participants performed 192 reaching trials in the CW force field. Participants were instructed to make fast, accurate movements to targets. To encourage consistent movement times, participants were informed that they moved too fast if movement time was less than 420 msec, and too slow if movement time was greater than 520 msec. These criteria were used only to provide participants with feedback about the consistency of their movements, and were not used to exclude data from the analysis.

Table 1. Learning Conditions and Design

Learning Condition Group	Sequence of Events			
	Training	Observation	rTMS	Test
No-Observation, No-TMS Control ($n = 12$)	Null field	None (10-min delay)	None (20-min delay)	CWFF
CCWFF Control ($n = 12$)	Null field	CCWFF	None (20-min delay)	CWFF
CCWFF rTMS-M1 ($n = 6$)	Null field	CCWFF	M1	CWFF
CWFF Control ($n = 12$)	Null field	CWFF	None (20-min delay)	CWFF
CWFF rTMS-M1 ($n = 6$)	Null field	CWFF	M1	CWFF
CWFF rTMS-SFL ($n = 6$)	Null field	CWFF	SFL	CWFF
CWFF Muscle Control ($n = 10$)	Null field	CWFF	None (20-min delay)	CWFF
CWFF Muscle rTMS ($n = 10$)	Null field	CWFF	Extensor carpi radialis	CWFF

Data Analysis

All data analyses were conducted using MATLAB (The Mathworks, Natick, MA) and SPSS software (SPSS, Chicago, IL). We measured the extent to which the CWFF perturbed participants reaching by measuring the maximum perpendicular distance between the hand and the line defined by the central start position and the target in question. Peak hand tangential velocity was also assessed to confirm that the magnitude of the velocity-dependent perturbation did not differ between groups. For each of the dependent variables, mean values were computed over successive and exclusive windows of 32 movements. Changes in performance over trials were tested by submitting movement curvature measures to a 6-Learning condition (CCWFF-Control, CCWFF-rTMS-M1, CWFF-Control, CWFF-rTMS-M1, CCWFF-rTMS-SFL, No-TMS, No-Observation Control) by 6-Movement trial bin (6 bins of 32 trials) mixed analysis of variance (ANOVA). Initial differences in movement curvature following observation and rTMS treatments were evaluated by submitting the mean movement curvature from the initial 32-trial bin to a 6-way learning condition (CCWFF-Control, CCWFF-rTMS-M1, CWFF-Control, CWFF-rTMS-M1, CCWFF-rTMS-SFL, No-TMS, No-Observation Control) between-subjects ANOVA. Given the results of previous experiments from our lab (Cothros et al., 2006; Mattar & Gribble, 2005), we were confident about our ability to predict the direction of differences between our TMS learning-condition groups and their respective force-field observation control groups. Consequently, we felt that Tukey's HSD was a suitably conservative test for evaluating the differences between learning-condition means.

RESULTS

Force Field Observation Influenced Force Field Performance

Over the course of the CWFF test, all participants adapted their reaching to compensate for the force field ap-

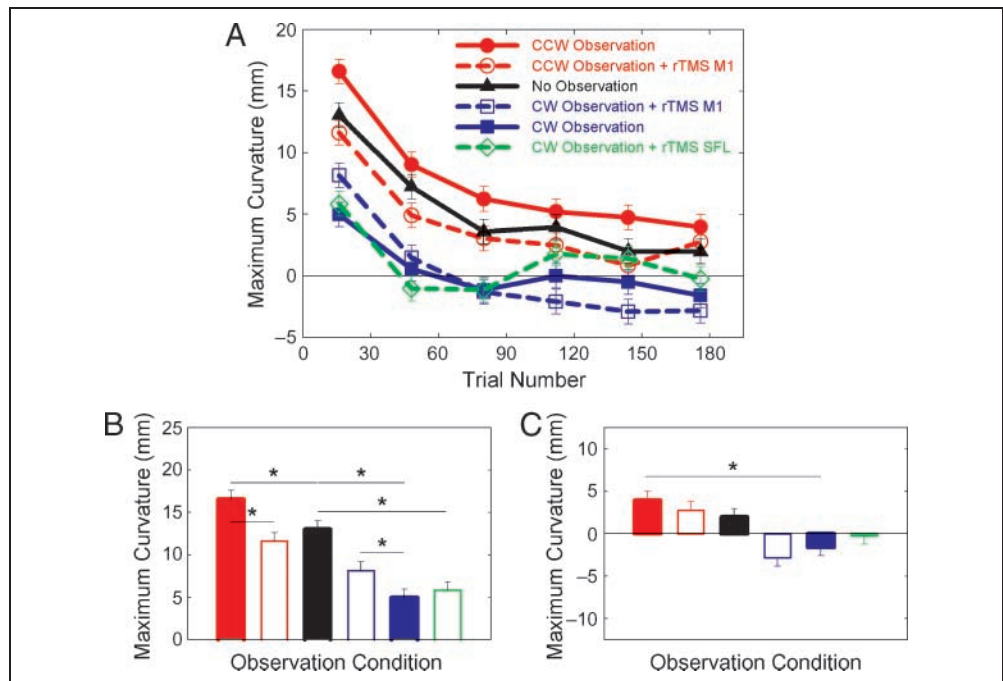
plied to the hand. This adaptation is evident in Figure 2A, which shows mean maximum movement curvature in the CWFF test as a function of trial number. Early in training, hand paths were highly curved and the degree of curvature depended both on whether the participant observed congruent (CWFF) or incongruent (CCWFF) forces, and on whether or not the participant received rTMS. Late in training, mean hand paths were significantly straighter, indicating that participants had learned to compensate for the CWFF. Overall, there was a significant reduction in movement curvature over the course of training [$F(5, 65) = 92.11, p < .001$], indicating that all participants learned to compensate for the CWFF.

The degree of initial movement curvature depended on whether participants observed the congruent CWFF or incongruent CCWFF video, and on whether or not they received a treatment of rTMS to M1, as indicated by a main effect for learning condition [$F(5, 1528) = 26.21, p < .001$]. Figure 2B shows mean maximum curvature during early exposure to the CWFF (averaged over the first 32 trials) as a function of experimental condition. Participants who observed CCWFF-learning produced movements with significantly higher curvature than participants in the no-observation control group (HSD: $p = .005$), whereas participants who observed CWFF-learning displayed significantly lower curvature than participants in the no-observation control group (HSD: $p < .001$). These results show that observing congruent or incongruent forces significantly influenced participants' initial ability to compensate for the CWFF perturbation, and replicate the results of Mattar and Gribble (2005).

rTMS to M1 Interferes with Motor Learning by Observing

The application of rTMS to M1 significantly interfered with both the detrimental and beneficial effects of observation on motor performance (see Figure 2B). Participants

Figure 2. Trajectory curvature for each learning condition. (A) Mean learning curves for participants tested in the CWFF after no observation (black, solid line), CCWFF-observation (red solid line), CWFF-observation (blue solid line), CCWFF-observation plus rTMS to M1 (red dashed line), CWFF-observation plus rTMS to M1 (blue dashed line), and CWFF-observation plus rTMS to the superior frontal lobule (green dashed line). Each point represents mean performance over 32 trials, and error bars represent one standard error of the mean. (B and C) Mean performance by each group over the first and last 32 trials of exposure to the CWFF, respectively. Error bars represent one standard error of the mean.



who received rTMS after observing CCWFF-learning showed significantly lower mean maximum curvature (they performed better) than participants who observed CCWFF-learning but did not receive rTMS (HSD: $p < .001$). In fact, their performance was not significantly different than controls in the no-observation group (HSD: $p > .10$). That is, rTMS eliminated the detrimental effect of observing learning in the incongruent force field. Conversely, participants who received rTMS to M1 after observing CWFF-learning showed significantly greater mean maximum curvature (they performed worse) than participants who observed CWFF-learning and did not receive rTMS (HSD: $p = .030$). Thus, rTMS to M1 interfered with the beneficial effect of observing the congruent force field.

The effect of observation continued, but was reduced, as physical practice continued in the CWFF test. Figure 2C shows mean maximum curvature toward the end of exposure to the CWFF (the last 32 trials) as a function of experimental condition. At the end of training, there was still a significant effect of observation on mean maximum movement curvature [$F(5, 1528) = 9.98, p < .001$]. Participants who observed CCWFF-learning performed worse than participants who observed CWFF-learning (HSD: $p < .001$). At the end of the CWFF test, groups receiving treatments of rTMS no longer differed from their no-TMS comparison groups (HSD: all $ps > .825$).

It is possible that rTMS interfered with learning by observing not because applying rTMS to the motor cortex interfered with learning in the motor cortex, but because rTMS was an unusual experience that simply caused participants to forget the information they acquired during observation. To control for the latter possibility, we con-

ducted an additional experiment in which we applied rTMS to a cortical control site (the SFL) after observation of CWFF-learning. If rTMS causes general forgetting, applying rTMS to the control site should also interfere with the beneficial effect of observing CWFF-learning. In contrast, if the effects of rTMS to M1 are due to interference with learning mechanisms in M1, then applying rTMS to the control site should have no effect on reaching performance. Our results agree with the latter case: Participants who received a treatment of rTMS to the SFL after observing CWFF-learning performed no differently than participants who received no rTMS after observing the CWFF (HSD: $p = .527$) and they performed significantly better than participants in the no-observation control group (HSD: $p < .001$).

It is possible that rTMS interferes with previously learned force-field information not because applying rTMS to the motor cortex interfered with learning in the motor cortex, but because suprathreshold rTMS results in stimulation-dependent contractions and movements of the contralateral limb. These contractions may act like a distractor that interferes with memory during the period intermediate to the learning and test portions of the experiment. We tested this possibility by running an additional control experiment. Twenty participants watched the CWFF movie before completing either (1) a no-rTMS rest period lasting 20 min or (2) a 15-min period in which 1-Hz rTMS was applied to the muscle belly of the extensor carpi radialis muscle. We aimed for this wrist extensor, but for some subjects, partially because of the size of the coil, the pulse was applied to the finger extensors (we observed both wrist and finger extensions). Pulse intensity was adjusted so that painless

muscle twitches were felt on every pulse (intensity ranged between 22% and 30%). Both groups of participants then completed 192 reaching trials while exposed to the CWFF. The results showed that rTMS is not simply acting like a distractor, as initial movement curvature for the resting control group ($11.41 \pm 1 SE$) was not significantly different from that for the muscular-rTMS group ($13.4 \pm 1 SE$) [$F(1, 598) = 2.61, p = .102$; see Figure 3]. This finding suggests that the mechanism by which rTMS interferes with observation-based learning about force fields does not depend on the distracting side effects of M1 stimulation.

As an additional check of our experimental manipulation, we analyzed the variability of movement curvature data between groups and found a significant main effect for learning condition [$F(5, 46) = 7.89, p < .001$]. We found that although the variability was larger for participants who watched the CCWFF rather than the CWFF movie (HSD: $p < .001$), perhaps because incongruence produces more variable performance than congruence, within each of these movie types, participants who received rTMS were no more or less variable than participants who did not receive rTMS (CWFF observation, HSD: $p = .732$; CCWFF observation, HSD: $p = .062$). This analysis suggests that our comparisons between the rTMS groups and their critical control groups are not hindered by between-group differences in variability.

Although unlikely (Cothros et al., 2006; Muellbacher et al., 2002), it is possible that rTMS to M1 did not interfere with recently acquired neural representations of forces in M1, but instead merely disrupted basal movement performance, that is, the general ability to control rapid limb movements. One argument against this possibility is the finding that participants who received rTMS after observing CCWFF-learning performed

better (were less affected by exposure to the CWFF perturbation) than participants who observed the same CCWFF-learning but who did not receive rTMS to M1. The finding that rTMS was associated with improved performance is inconsistent with the idea that rTMS interfered more generally with basal motor control.

To further rule out this possibility, we compared three measures of basal movement performance over the first 32 trials of exposure in the CWFF test for subjects receiving rTMS to M1 with those for subjects who did not receive rTMS. First, to assess the ability of subjects to generate appropriately rapid movements, we computed mean peak hand tangential velocity, which did not differ as a function of learning condition [$F(5, 1528) = 0.49, p = .782$]. Because the magnitude of the force applied during the perturbation was tied to the instantaneous velocity of the movement trajectory, this analysis also served to check that all groups experienced the same magnitude of force perturbations in the CWFF test. Second, to assess temporal consistency, we computed mean time to peak velocity, which also did not differ between rTMS and control groups (HSD: $p > .10$). Finally, to assess more general spatio-temporal aspects of trajectory smoothness, we computed root-mean-squared jerk (Flash & Hogan, 1985) for each movement. Again, no significant differences were observed for rTMS versus control groups (HSD: $p > .10$).

Another method for ruling out the possibility that rTMS disrupted basal movement performance would be to compare the performance of our no-observation group to the performance of an additional no-observation group who received an application of rTMS before being exposed to the force field. Indeed, we have compared these two conditions in our lab (Cothros et al., 2006) and found that rTMS did not affect the size of the initial error or the rate of learning of a perturbing force field. Together, these three pieces of evidence reinforce the notion that rTMS does not degrade basal motor performance. Instead, rTMS affects performance by interfering with previously learned motor information.

DISCUSSION

We have demonstrated that rTMS applied to the primary motor cortex (M1) interferes with motor learning by observing. As in Mattar and Gribble (2005), we found that reaching performance in the CWFF test benefited from prior observation of an actor reaching in the congruent CWFF, and was detrimentally affected by prior observation of an actor reaching in the CCWFF. We also found that a 15-min treatment of 1 Hz rTMS applied to M1 in the interval between observation and the CWFF test interfered with the beneficial effect of observing reaching in the CWFF, and even more dramatically, removed altogether the detrimental effect of observing reaching in the CCWFF. In contrast, applying rTMS to a cortical

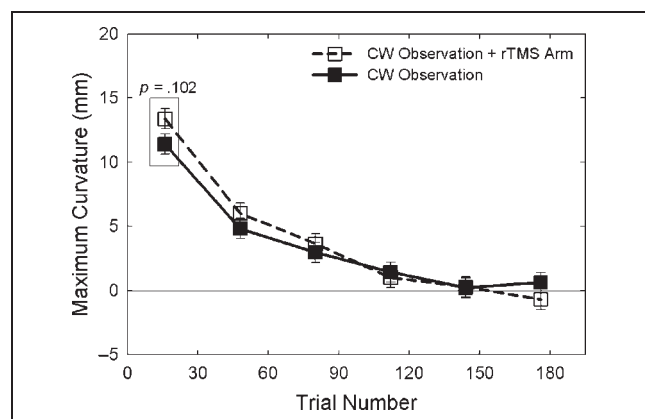


Figure 3. Trajectory curvature for control experiment in which rTMS was applied to the extensor carpi radialis. Mean learning curves for participants tested in the CWFF after CWFF-observation (black solid line) and CWFF-observation plus rTMS to the wrist extensors of the right arm (black dashed line). Each point represents mean performance over 32 trials, and error bars represent one standard error of the mean.

control site, or directly to the muscles controlling the right wrist, did not influence the motor learning by observing effect. These findings support the hypothesis that action observation engages learning mechanisms in the primary motor cortex.

The idea that learning mechanisms in the motor system are engaged by observing the actions of others was proposed by Mattar and Gribble (2005), who found that performing unrelated arm movements during observation—thereby occupying the motor system and presumably interfering with the engagement of reach related learning mechanisms—reduced the effectiveness of observation on later performance. They argued that observation engages areas in the motor system that would be active during performance, and therefore, observation allows the motor system to build a neural representation of the observed force field environment. This representation may be used to adapt the neural signals controlling the magnitude and timing of muscular activation to compensate for the force field. Here we provide more direct evidence in support of this hypothesis: The application of rTMS to the motor cortex interfered with observation-related learning, whereas the application of rTMS to a cortical control site had no effect on reaching performance after observation. Given that observation could potentially induce changes in the system at many different levels, it is noteworthy that learning mechanisms are engaged at the level of the primary motor cortex.

In a related study, observation of directional thumb movements increased the likelihood that short trains of high-frequency rTMS applied to M1 would elicit thumb movements in the same direction (Stefan et al., 2005). Whereas this thumb movement study demonstrates that observation can prime the choice of movement direction, the present force learning study demonstrates that relatively low-level information about a perturbing force field is encoded by M1 during observation.

Several other recent studies have used rTMS to explore the role of M1 in early learning about forces in the motor system. rTMS applied to M1 interfered with participants' ability to learn to modulate grip forces associated with differently weighted novel objects (Chouinard, Leonard, & Paus, 2005). Muellbacher et al. (2002) used a finger-pinching task to demonstrate that rTMS applied to M1 interferes with participants' ability to retain improvements made during earlier practice. Finally, Cothros et al. (2006) showed that applying rTMS to M1 had dual effects: It both interfered with participants' ability to retain force information acquired during a recently practiced force-field reaching task, and also reduced the extent to which recently learned force information interfered with the acquisition of new force patterns. These studies are consistent with the idea that the primary motor cortex plays a critical role in acquiring and retaining information about how to execute movements involving novel patterns of force production.

Evidence suggests that M1 may play a special role in learning new mappings between hand trajectories and limb dynamics. Electrophysiological recordings in monkey have shown that M1 neurons change their firing patterns in response to practice in externally applied force fields (Li, Padoa-Schioppa, & Bizzi, 2001; Gandolfo, Li, Benda, Padoa-Schioppa, & Bizzi, 2000), joint-specific viscous loads (Gribble & Scott, 2002), constant bias forces (Kalaska, Cohen, Hyde, & Prud'homme, 1989), and visuomotor rotations (Paz, Natan, Boraud, Bergman, & Vaadia, 2005). Functional brain imaging studies have established that M1, in addition to other motor system brain areas, plays a key role in human motor learning about new movement sequences (Karni et al., 1998), visuomotor rotations (Paz, Boraud, Natan, Bergman, & Vaadia, 2003; Grafton, Salidis, & Willingham, 2001), and externally applied force fields (Shadmehr & Holcomb, 1997). Moreover, low-frequency rTMS applied to the motor cortex can interfere with learning of tasks that involve the acquisition of new relationships between kinematics and dynamics (Cothros et al., 2006; Chouinard et al., 2005; Muellbacher et al., 2002). Although it is highly unlikely that M1 is the only site of motor learning in these cases, M1 plays a critical role in learning new relationships between movement kinematics and forces.

How are learning mechanisms in M1 accessed by action observation? This is an important question to consider because, as far as we know, the motor cortex does not receive direct input from the visual cortex (Watkins et al., 2003). Motor learning by observing can be linked to mirror neurons, discovered in the monkey ventral premotor cortex (PMv; Gallese et al., 1996; Rizzolatti et al., 1996; Di Pellegrino et al., 1992), and the inferior parietal cortex (Brodmann's area 7b; Fogassi et al., 2005; Gallese et al., 2002), which increase their activity both when a monkey performs a goal-directed action and observes the same or similar actions (Gallese et al., 1996). Importantly, the PMv is directly connected both to the spinal cord and to the primary motor cortex, and it is these cortico-cortical connections that have been linked to changes in the neural excitability of the motor cortex when human observers watch or listen to another person performing a goal-directed action, as measured by the amplitude of MEPs elicited by single-pulse TMS applied to M1 (Patuzzo et al., 2003; Watkins et al., 2003; Baldissera et al., 2001; Gangitano et al., 2001; Strafella & Paus, 2000; Fadiga et al., 1995). Functional brain imaging studies have also demonstrated that M1 is activated during action observation (Shmuelof & Zohary, 2005, 2006; Buccino et al., 2001).

There are a number of issues worth noting. Of course, observational learning may happen simultaneously at any or all components of the visuomotor system, including the premotor cortex, the dorsal lateral prefrontal cortex, and the cerebellum (Petrosini, 2007; Torriero, Oliveri, Koch, Caltagirone, & Petrosini, 2007), and the level at which learning is most evident may depend

critically on the nature of the task. In the present study, the engagement of learning mechanisms in the motor cortex may be tied to the fact that our task involved learning about novel forces. Although several cortical motor areas, including M1, code movement distance and direction, the primary motor cortex is important for representing force at the cortical level. Electrophysiological recordings in monkey have shown that whereas both the premotor and primary motor cortex are tuned to movement direction both at the single cell level (Sergio, Hamel-Paquet, & Kalaska, 2003; Caminiti, Johnson, Galli, Ferraina, & Burnod, 1990; Kalaska et al., 1989; Georgopoulos, Schwartz, & Kettner, 1986; Thach, 1978) and the population level (Georgopoulos et al., 1986), neural activity in the primary motor cortex is related to movement direction, force direction, force magnitude, the rate of change of force magnitude (Thach, 1978; DeLong & Strick, 1974; Evarts & Thach, 1969; Evarts, 1968), and to higher-order dynamical variables such as joint power (Scott, Gribble, Graham, & Cabel, 2001). Given that force coding appears to be the domain of the primary motor cortex, it is possible that observation engaged learning mechanisms in M1 because adaptation was driven by the need to learn a new relationship between hand kinematics and limb dynamics.

It is important to recognize that there was likely some diffusion of current generated by the TMS pulse from M1 to nearby brain areas. If observation engages learning mechanisms in brain areas immediately neighboring the motor cortex treatment site, rTMS may interfere with learning at these sites via lateral spread of electrical activity. The likelihood of this possibility is low, however, because muscle-specific effects have been demonstrated using TMS (Strafella & Paus, 2000). Another feature of TMS is that the effects of treatment at one brain site can be detected at other brain sites via their neural connections (Chouinard, Van Der Werf, Leonard, & Paus, 2003; Paus, 1999). Because many of the motor system brain areas located on the dorsal and ventral-lateral surface of the frontal lobe have direct connections to M1, these motor system areas may have been remotely affected by rTMS to M1 via these neural connections. The likelihood that effects at remote sites can account for our findings is low, however. Chouinard et al. (2003) have shown that applying rTMS to the dorsal premotor cortex did not interfere with how participants adapted their grip force to the weights of new objects, whereas applying rTMS to M1 did interfere with this adaptation. These findings suggest that M1 plays a special role in learning about forces, and that the interference induced by rTMS is relatively focal.

Our results are consistent with what is known about the relationship between the mirror system and the motor system. Mirror cells are found in brain areas known to contribute to the control of goal directed actions, and action observation alone can engage the neural systems that control action performance. Behavioral

evidence from our lab suggests that observing others learning to compensate for a perturbing force field influences how an observer deals with that force field, suggesting that action observation can engage learning mechanisms in the motor system. The results presented here replicate these prior results, and provide new evidence that one site of motor learning by observing is the primary motor cortex. In future studies, the differential roles that frontal and parietal mirror neuron sites play in observational learning will be explored.

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