Parietal rTMS Disrupts the Initiation but not the Execution of On-line Adjustments to a Perturbation of Object Size

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Abstract

■ Previous studies have implicated the human parietal lobes in the on-line guidance of action. However, no study to date has examined at what stage in the on-line adjustment process do the parietal lobes play their most critical role. Repetitive transcranial magnetic stimulation (rTMS) was applied over the left intraparietal sulcus as participants reached to grasp a small or large illuminated cylinder. On some trials, the illumination could suddenly switch from the small to large cylinder, or vice-versa. Small–Large switches were associated with relatively early grip aperture adjustments, whereas Large–Small switches were associated with relatively late grip aperture adjustments. When rTMS was applied early in the movement, it disrupted on-line adjustments to Small–Large target switches, but not to Large–Small switches. Conversely, when rTMS was applied late in the movement, it disrupted adjustments to Large–Small target switches but not to Small–Large switches. The timing of the disruption by rTMS appeared linked to the initiation of the adjustment. It was concluded that the left parietal lobe plays a critical role in initiating an on-line adjustment to a change in target size, but not in executing that adjustment. The implications of these results for current views of on-line control are discussed. ■

INTRODUCTION

To examine the various roles of the parietal lobes in action, a useful distinction may be made between the premovement (or "planning") stage of an action, and the on-line (or "control") stage (Glover, 2003, 2004; cf. Woodworth, 1899). On the one hand, the planning stage appears to involve the selection of a motor program from among several possible alternatives, on the basis of a visual analysis of the target's features, as well as a consideration of the overarching goals of the action. The incorporation of a wide variety of visual and cognitive information enables the planning system to select a movement that is reasonably close to that required for achieving the goals of the movement.

On-line control, on the other hand, is thought to operate in a relatively rapid fashion, on the basis of a fast analysis of the visuospatial features of the target in relation to the effector, in conjunction with an efference copy. Whereas planning has often been found to be subject to conscious influence (e.g., Klatzky, Pellegrino, McCloskey, & Doherty, 1989; Klatzky, McCloskey, Doherty, Pellegrino, & Smith, 1987), on-line adjustments generally appear to precede conscious awareness of a change in the target (Castiello & Jeannerod, 1991) and can even operate outside of any conscious awareness (Glover & Dixon, 2002; Savelsbergh, Whiting, & Bootsma, 1991; Goodale, Pelisson, & Prablanc, 1986). Given these distinctions between planning and control, one may consider control as a separate stage of action from planning, and possibly one that involves a specific subset of the parietal regions involved in action. In the present study, we show that an area of the left posterior parietal lobe of humans, bordering on the intraparietal sulcus (IPS) is crucial in the on-line control of a reaching and grasping action. In particular, we show that this area plays a critical role in the initiation of on-line adjustments to a change in target size.

Role of the Parietal Lobes in On-line Control

Both PET and fMRI studies have implicated the parietal lobes in actions including both body and eye movements (Astafiev et al., 2003; Connolly, Goodale, DeSouza, Menon, & Vilis, 2000), and a further delineation between reaching and grasping areas of the parietal lobes may also be possible, with reaching generally believed to invoke more posterior regions and grasping more anterior regions (Binkofski et al., 1998; Grafton, Arbib, Fadiga, & Rizzolatti, 1996). However, until recently, very few studies have tried specifically to examine the role of the parietal lobes in on-line monitoring and control. The drawbacks of using PET or fMRI to do this are obvious, on the basis of the lack of fine temporal resolution, which

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limits the abilities of such techniques to isolate planning and/or control, although some efforts have nonetheless been made.

Desmurget, Grea, et al. (2001) used PET to examine the regions of the brain active during the on-line adjustment of pointing movements made to targets that could change position coincident with movement initiation. This type of paradigm (the ''perturbation paradigm'') allowed Desmurget, Grea, et al. to examine on-line processes, as the occurrence of changes in target position was unpredictable. Thus, any adjustment to the new position of the target required an on-line monitoring of target position followed by a change in the ongoing motor program that would bring the hand to the new position of the target. Desmurget, Grea, et al. found that an area within the IPS region was more active on the trials in which large on-line adjustments were required than on trials where no such adjustments had to be made (i.e., when the target position remained stable).

A transcranial magnetic stimulation (TMS) study by Desmurget, Epstein, et al. (1999) using the same paradigm as that used by Desmurget, Grea, et al. (2001) found that disruption of a similar IPS region impaired the on-line adjustments that normally take place to a change in target position. This finding nicely complemented that reported in the Desmurget, Grea, et al. PET study.

Finally, recent work with an optic ataxic subject (Pisella et al., 2000) has illustrated the important role of the parietal lobes in making on-line adjustments to a change in target position. The optic ataxic I. G. suffers from extensive bilateral damage to the posterior parietal lobes, including large portions of the superior parietal lobe (SPL) and the adjacent IPS, and a somewhat smaller portion of the inferior parietal lobe (IPL). Pisella et al. (2000) examined I. G.'s ability to make on-line adjustments in pointing to a target that changed position coincident with movement initiation. Even though I. G. was nearly as accurate as controls in pointing to a stationary target, she was nevertheless unable to make the fast, automatic adjustments that healthy subjects made when the target changed position at movement onset (Pisella et al., 2000). Similarly, I. G. was also found to be impaired at making on-line adjustments in a grasping task: When the target suddenly moved, I. G. first made one grasping movement to the original position of the target, then made a distinct second movement to the new position of the target (Grea et al., 2002). This type of behavior was not seen in healthy controls, who quickly and easily adapted their movements on-line to the new location of the target.

Taken in sum, a fairly consistent set of results suggest not only that the parietal lobes are heavily involved in the on-line monitoring and adjustment of actions, but also that more specific regions in the parietal lobes (possibly including the IPS and neighboring regions of the superior parietal cortex) play a crucial role in the control phase.

The Size–Perturbation Paradigm

In the present study, we sought to further examine the role of the parietal lobes in the on-line control phase of action. We did so using a size–perturbation paradigm originally employed by Paulignan, Jeannerod, MacKenzie, and Marteniuk (1991). That study utilized an apparatus consisting of a narrow cylinder nested inside a larger cylinder, situated within a darkened room. The cylinder to be grasped was lit from beneath at the onset of the trial, making it the only visible target. On some trials, the target cylinder was switched (by extinguishing its illumination and illuminating the other cylinder) coincident with movement onset. On those trials, subjects then had to adjust their grasping movements to the new size of the cylinder. As the grip aperture (i.e., distance between thumb and forefinger) is scaled to the size of the target from very early in a reaching movement (e.g., Glover & Dixon, 2002; Jakobson & Goodale, 1991; Jeannerod, 1984), a change in target size requires a rescaling of the grip aperture on-line in order to ensure a successful grasp. That is, if the target suddenly changes from small to large, the original plan of the movement (i.e., a relatively small grip aperture) must be modified in flight in order to accommodate the new size of the cylinder (i.e., a relatively large grip aperture). Conversely, if the target suddenly changes from large to small, the original plan of the movement (a large grip aperture) must be modified to accommodate the new, small target.

Using this size–perturbation paradigm to examine on-line control in healthy subjects, Paulignan, Jeannerod, et al. (1991) showed that the temporal parameters of the in-flight modifications in grip aperture depended on whether the perturbation was from a small-to-large (Small–Large) target or from a large-to-small (Large–Small) target. Whereas Small–Large perturbations led to a relatively early increase in grip aperture (within 350 msec), Large–Small perturbations led to a relatively late initiation of the adjustment (approximately 450 msec). The distinct timing of these corrections suggests that the size perturbation paradigm offers a unique opportunity to examine the role of the parietal lobes in the on-line correction of actions. In particular, by disrupting parietal lobe activity using repetitive TMS (rTMS) at different times in the movement, it ought to be possible to examine at which stage in the control process the parietal lobes play the most crucial role.

Two hypotheses may be considered. First, if the IPS region is crucial in initiating on-line corrections, then disrupting its activity using rTMS should have its greatest effect when the disruption coincides with the initiation of the correction. Specifically, rTMS applied early in a movement should affect the adjustments that are initiated early (i.e., in the Small–Large perturbation condition), but—assuming that the effect of rTMS is short lasting—leave adjustments made later in the movement (i.e., in the Large–Small condition) unaffected. The reverse should also hold: rTMS applied late in the movement should affect adjustments initiated late (Large–Small condition), but not adjustments initiated early (Small–Large condition). We will hereafter refer to this as the "initiation" hypothesis.

An alternate hypothesis is one that supposes that the IPS is involved in the entire process of on-line monitoring and adjustment. Under this hypothesis, a disruption of parietal lobe activity ought to lead to a noticeable disruption in any on-line corrections underway during the time of the disruption, regardless of whether they have already been initiated or not when the rTMS begins. Similar to the first hypothesis, this hypothesis also predicts that rTMS applied early ought to impair on-line adjustments in the Small–Large condition (as these begin early). However, this hypothesis differs from the first hypothesis in predicting that rTMS applied late ought to impair on-line adjustments in both the Small–Large condition (where the adjustments begin early but continue throughout the movement) and the Large–Small condition (where the adjustments begin late). We will hereafter refer to this as the "execution" hypothesis.

Previous examinations of the role of the IPS in on-line control, although useful in showing a general role, could make no distinction between the "initiation" and "execution" hypotheses, as neither the timing of the disruption (Desmurget, Epstein, et al., 1999) nor the timing of the adjustment (Desmurget, Grea, et al., 2001; Desmurget, Epstein, et al., 1999) were manipulated. In contrast, the present study was set up specifically to test the "initiation" and "execution" hypotheses regarding the role of the IPS in the on-line monitoring and adjustment of actions.

RESULTS

Behavioral Results

In order to determine the validity of the size perturbation paradigm for testing adjustments that begin early versus those that begin late, we conducted a preliminary analysis of the timing of the perturbation effects. In particular, we determined whether the Small–Large perturbation would have an earlier affect on grip than the Large–Small perturbation, as it had in Paulignan, Jeannerod, et al. (1991). In order to increase the power of our analysis, data from the non-TMS trials in both experiments were collapsed together in a single analysis.

Figure 1 compares grip aperture (left) and velocity of grip aperture (right) in the control (no TMS) Small trials and control (no TMS) Small–Large trials. The first statistically significant difference between the two conditions occurred for grip velocity at 45% of movement time, $t(11) = 2.88$, $p < .05$. Movement times in the two conditions did not differ statistically, $t(11) = 1.42$, $p > .05$ (see Table 1). Figure 2 shows grip aperture (left) and velocity of grip aperture (right) in the Large trials and Large–Small trials. The first statistically significant difference between the two conditions occurred for grip velocity at 60% of movement time, $t(11) = 2.76$, $p < .05$. Movement times in the two conditions

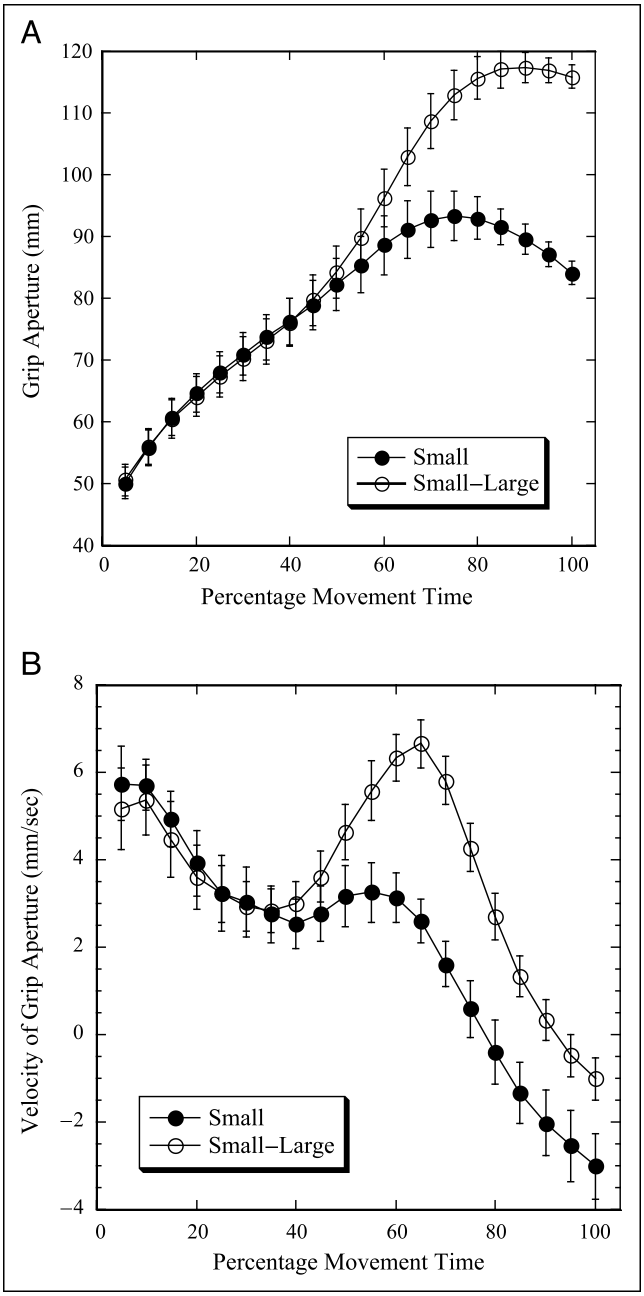


Figure 1. Effect of target initial size and perturbation condition on grip aperture (A) and velocity of grip aperture (B) over time in the control (no rTMS) conditions for Small and Small–Large trials, collapsed across experiments. The *x*-axis represents normalized time in 5% increments.

Table 1. Movement Times by Initial Size and Perturbation Condition in Control (Non-TMS) and TMS Conditions in Experiments 1 and 2

Initial size/ Perturbation	*Small*		*Large*		*Small-to-Large*		*Large-to-Small*	
	Ctrl	*TMS*	*Ctrl*	*TMS*	*Ctrl*	*TMS*	*Ctrl*	*TMS*
Experiment 1	497.6 (15.9)	506.2 (24.4)	489.6 (18.5)	494.7 (19.6)	492.4 (23.0)	491.4 (26.8)	491.0 (21.1)	501.0 (21.0)
Experiment 2	490.2 (15.8)	506.9 (22.6)	481.0 (17.3)	486.9 (18.4)	493.1 (18.6)	510.2 (21.9)	501.4 (22.6)	497.6 (19.8)

(Standard errors in parentheses).

did not differ statistically, $t(11) = 0.85$, $p > .05$ (see Table 1).

These data showed that the Small–Large perturbation led to an earlier initiation of the adjustment than did the Large–Small perturbation (at 45% and 60% of movement time, respectively). Thus, we concluded that our setup had the desired effect of leading to one adjustment that was initiated relatively early in the movement and another adjustment that was initiated relatively late the movement.

TMS Results: Experiment 1

This tested the effect of rTMS of the left IPS presented during the first half of movement. Data from the four types of trials (Small, Large, Small–Large, and Large–Small) in Experiment 1 are shown for both control and TMS trials in Figure 3. The effects of TMS in each trial type are summarized in Figure 4. We conducted *t* tests of the differences in grip aperture between control and TMS trials for each trial type (Small, Large, Small–Large, and Large–Small) at each 20% of movement time. It is clear from Figure 3 (panel c) and Figure 4 that the TMS had its greatest effects between 40% and 60% of movement time in the Small–Large condition (all t's > 2.7, all $p < .05$). There was no consistent evidence of TMS effects at any other time in the movement for the Small–Large condition or at any times for the other three conditions (panels a, b, d of Figure 3 and Figure 4). Movement times did not differ between the control and TMS conditions in any of the four trial types (Small, Large, Small–Large, Large–Small), all $p > .05$.

The results of Experiment 1 clearly demonstrated that TMS applied over the SPL during the first half of the movement affected an adjustment that was initiated during the first half of the movement. This result was consistent with both the ‘‘initiation’’ and ‘‘execution’’ hypotheses, as both had predicted effects of TMS when the timing of the adjustments' initiation and TMS coincided. Experiment 2 was thus designed to provide a critical test of the two hypotheses. In particular, the ‘‘initiation’’ hypothesis would predict an effect of the TMS only in the Large–Small perturbation condition, as this was the condition in which the adjustment was initiated late in the movement. In contrast, the ‘‘execution’’ hypothesis would predict an effect of the TMS in both the Small–Large and Large–Small conditions, as both adjustments were ongoing during the latter stages of the movement.

TMS Results: Experiment 2

This tested the effect of rTMS of the left IPS presented during the second half of movement. During testing, the experimenter noticed that on several of the Large–Small trials with rTMS, the subjects actually erroneously grasped the large cylinder, even though it was no longer visible. This suggested that rTMS in the Large–Small condition affected the subjects' adjustments. Later examination of the data proved this to be the case.

Data from the four types of trials (Small, Large, Small–Large, and Large–Small) in Experiment 1 are shown for both control and TMS trials in Figure 5. The effects of TMS in each trial type are summarized in Figure 6. Effects of TMS were evident in the Large–Small condition (Figure 5, panel d and Figure 6), at 80% and 100% of movement time (all t's > 2.1, all $p < .05$). There was no consistent evidence for effects of TMS at any other time in the Large–Small condition, or in any other condition. Movement times did not differ between the control and TMS conditions in any of the four trial types (Small, Large, Small–Large, Large–Small), all $p > .05$.

The results of Experiment 2 supported the ‘‘initiation’’ hypothesis, in which the IPS is said to play its most critical role in the initiation of on-line adjustments. In particular, TMS over the IPS region had the greatest effect on the adjustment that was initiated in the second half of the movement (Large–Small) but did not affect the adjustment initiated in the first half of the movement (Small–Large). The results did not support the ‘‘execution’’ hypothesis, which would have predicted that the TMS would disrupt both the Large–Small and Small–Large adjustments, as both were ongoing during the time the TMS was applied.

DISCUSSION

The present study demonstrated the critical role of the IPS region in the initiation of on-line corrections. Here, we found that rTMS over the left IPS disrupted on-line

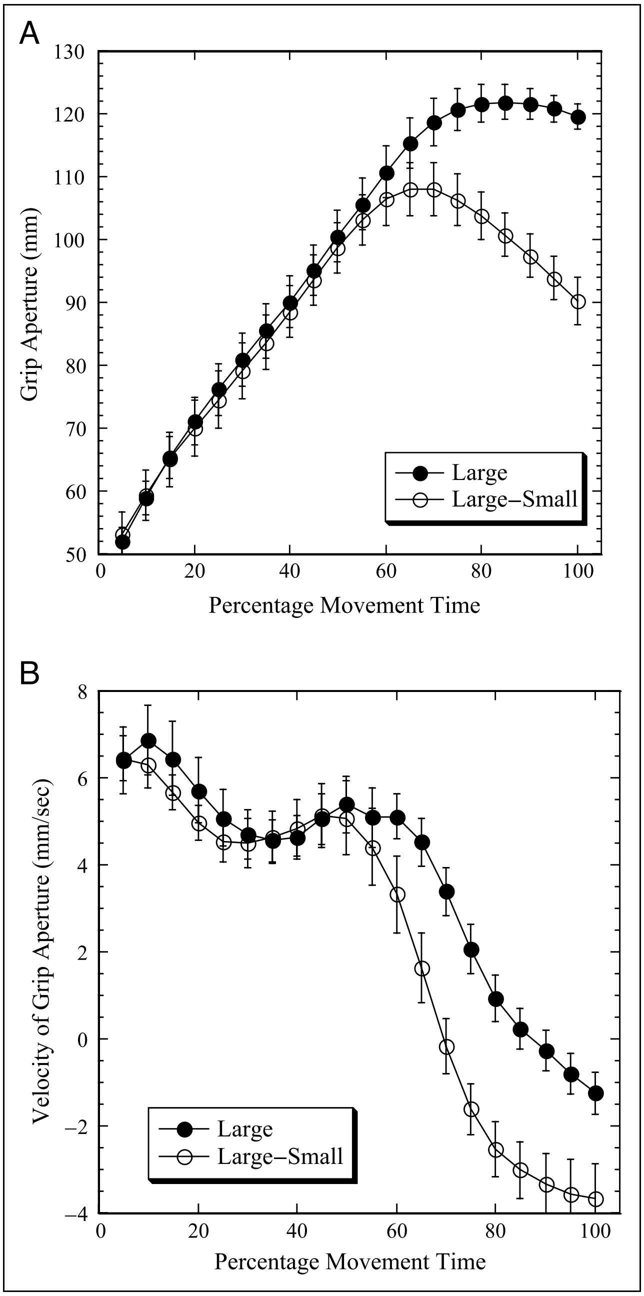


Figure 2. Effect of target initial size and perturbation condition on grip aperture (A) and velocity of grip aperture (B) over time in the control (no rTMS) conditions for Large and Large–Small trials, collapsed across experiments. The *x*-axis represents normalized time in 5% increments.

adjustments to a change in target size, however, this was true only when the rTMS was applied concurrent with the initiation of the adjustment. In contrast, when the rTMS was applied after the adjustment had already begun, it had no discernible impact on the ongoing adjustment process.

In Experiment 1, rTMS applied over the left IPS during the first half of the movement disrupted the Small–Large adjustment between 40% and 60% of movement time, but had no effect on the Large–Small adjustment at any time during the movement. This dissociation presumably occurred because the adjustment to the Small–Large perturbation was initiated during the first half of the movement while the rTMS was being applied. In contrast, the adjustment to the Large–Small perturbation was not affected, presumably because it only began in the second half of the movement, when the rTMS was no longer being applied.

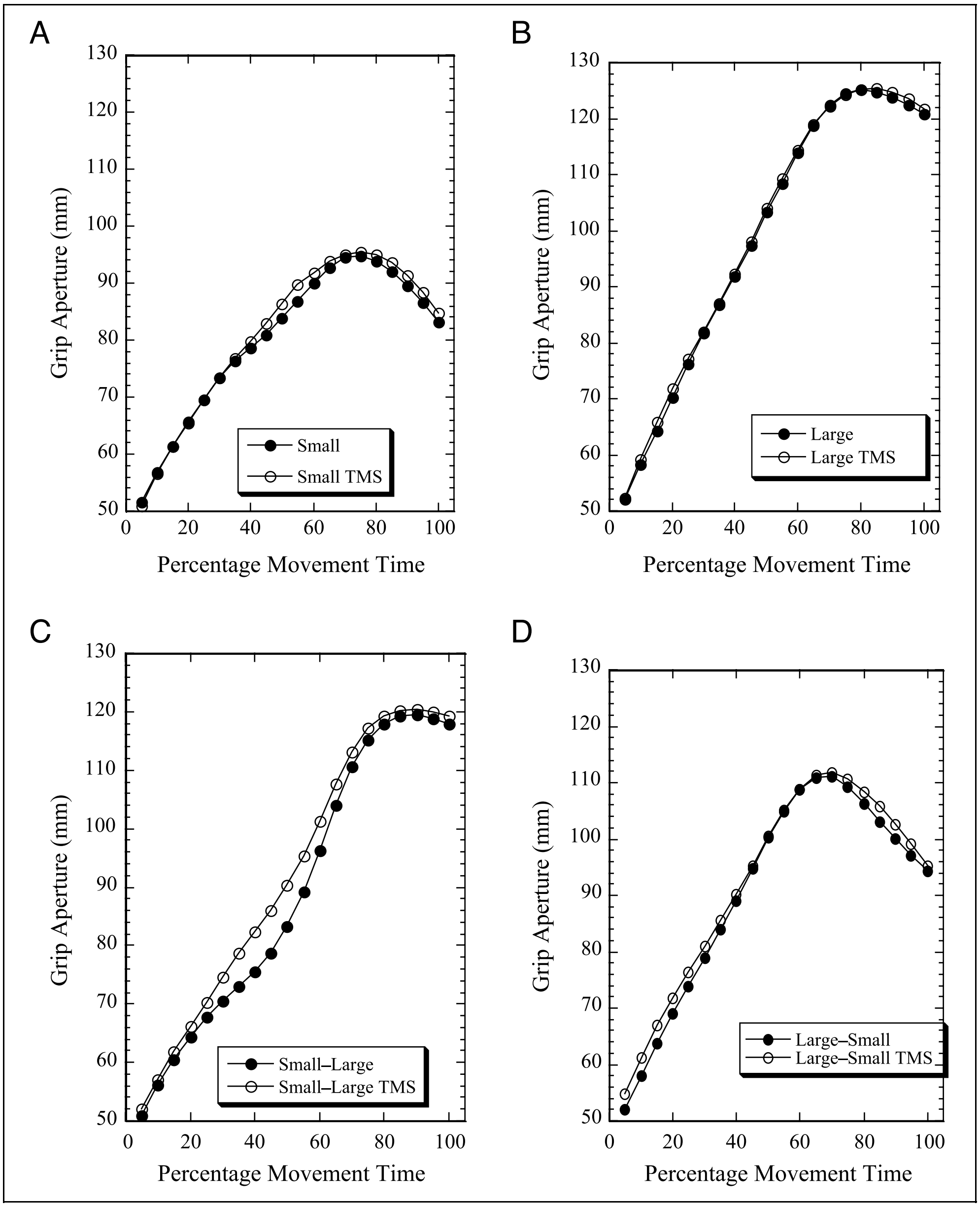
In Experiment 2, in contrast, rTMS applied over the IPS during the second half of the movement disrupted the Large–Small adjustment between 80% and 100% of movement time, but had no effect on the Small–Large adjustment at any time during the movement. Again, this presumably occurred because the adjustment to the Large–Small perturbation was initiated during the second half of the movement while rTMS was being applied. In contrast, the adjustment to the Small–Large perturbation was not affected, presumably because it was initiated in the first half of the movement, before rTMS was applied.

Taking both experiments in sum, it appears that the crucial role of the IPS region in on-line adjustments was in the initiation of the adjustment, and not its execution. One possibility is that adjustment execution is linked to other areas such as the primary motor cortex, basal ganglia, and cerebellum.

One point worth mentioning in regards to the results of Experiment 1 is that as in Paulignan, Jeannerod, et al. (1991), the Small–Large perturbation initially had a paradoxical effect on grip aperture (see Figure 1). That is, whereas the grip aperture ultimately had to *increase* to accommodate the new size of the target, the earliest effect was a *deceleration* of the grip aperture in the Small–Large condition relative to the Small condition. In the present study, this deceleration led to a grip aperture that was sometimes smaller in the Small–Large condition than at a corresponding time in the Small condition (Paulignan et al. did not directly compare grip aperture over time across conditions).

Whereas both studies observed a similar effect of the Small–Large perturbation on grip velocity, and this therefore appears to be the most robust effect of the perturbation, some differences did exist between their study and the present one. For example, Paulignan, Jeannerod, et al. observed that for three participants in the Small–Large condition, grip aperture first peaked at an amplitude consistent with the Small target, then rose again to an amplitude consistent with the Large target. In the present study, the deceleration in grip velocity in the Small–Large condition occurred while the grip aperture was still below that normally attained for the Small target, and this was the case for all participants. Although idiosyncratic responses to perturbations are not unheard of in motor control (van Sonderen, van der Gon, & Gielen, 1988), we can offer no reason why such responses occurred in some of Paulignan, Jeannerod, et al.'s participants but in none of ours.

Figure 3. Experiment 1: Grip aperture at each 5% of movement time for each trial type, comparing control and TMS trials. (A) Small target trials; (B) Large target trials; (C) Small–Large perturbation trials; (D) Large–Small perturbation trials. Note the large effect of the TMS between 40% and 60% of movement time in the Small–Large condition (C).



In the present study, the TMS seemed to eliminate the deceleration in the Small–Large condition (Figure 3), and so might be argued to actually be facilitating the adjustment rather than impairing it. Although such an interpretation may be intuitively appealing, we point out that the TMS nevertheless had the effect of producing a movement that was atypical inasmuch as the "normal" response to the adjustment (as observed both here and in Paulignan, Jeannerod, et al.) did not occur. Thus, we conclude that the effects of TMS were disruptive, despite the initially paradoxical nature of the Small–Large adjustment. This interpretation is also consistent with the results of Experiment 2.

Our results can be compared to another study of TMS and on-line control conducted by Desmurget, Epstein, et al. (1999). In that study, participants made speeded pointing movements to LEDs. On some trials, the position of the LEDs was shifted laterally coincident with the onset of the movement. Desmurget, Epstein, et al. noted an almost complete extinction of on-line adjustments when TMS was applied over the left IPS at movement onset.

In contrast, in our study the effects of TMS seemed more modest. Whereas there was some disruption of the adjustments, this disruption could be overcome when the TMS was applied early in the movement (Experiment 1), or was only evident in the second half of the movement (Experiment 2). One possibility is that the pointing task used by Desmurget et al. represented a simpler task than our grasping task and was thus more susceptible to the disruptive effects of TMS. Support for this notion comes from the fact that adjustments

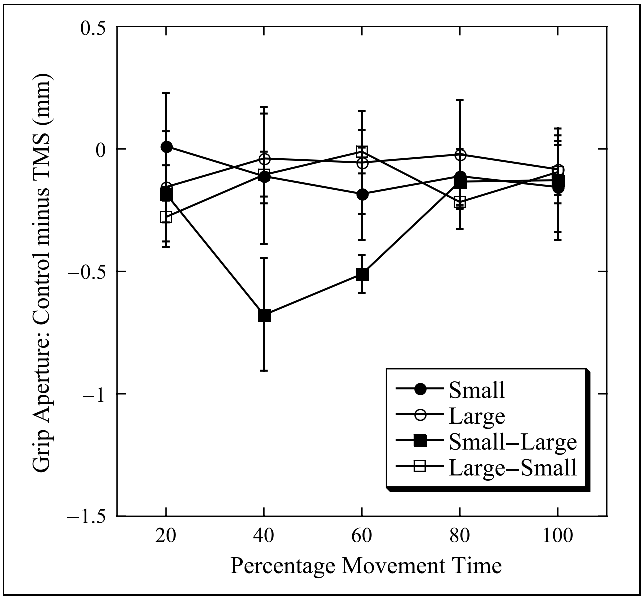


Figure 4. Experiment 1: Effects of TMS on grip aperture at each 20% of movement time for each trial type. Error bars represent standard errors of the mean.

in the pointing perturbation task used by Desmurget were initiated much sooner than were adjustments in the grasping perturbation task used here (~100 msec in pointing vs. ~225 and ~300 msec in the Small–Large and Large–Small conditions, respectively, in grasping). Further, in the Desmurget et al. study, the timing of the TMS was not manipulated; thus TMS effects would have been manifest when the adjustments were initiated. In the present study, however, the timing of the TMS was manipulated, and thus its effects on different adjustments were dissociable in time.

On-line Control and Adjustments to Perturbations

There have been several characterizations of on-line control put forward in recent years. For example, it has been argued that on-line control operates through a comparison of the effector with the desired state of the system (e.g., Meyer, Abrams, Kornblum, Wright, & Smith, 1988; Crossman & Goodeve, 1983). When a discrepancy is noted between the two, an error reduction mechanism comes into play. This type of model offers perhaps the simplest explanation of on-line control, yet fails in certain respects. For example, such a model cannot explain why grip aperture typically peaks larger than the size needed to grasp the target even when no target perturbation occurs (e.g., Glover & Dixon, 2002; Jakobson & Goodale, 1991; Jeannerod, 1984).

Another possible explanation for what occurs during on-line reactions to a perturbation of a target may be termed the "replanning" hypothesis (Paulignan, Jeannerod, et al., 1991, Paulignan, MacKenzie, et al., 1991). On this analysis, the change in target size requires a recomputation of the parameter of the grip aperture, and a subsequent reformulation of the plan required to grasp the target. Such a plan may then be vectorially added onto the existing plan, or may supersede the existing plan entirely. This hypothesis could be used to explain the paradoxical deceleration of grip aperture that occurred in the Small–Large condition of both Paulignan, MacKenzie, et al. (1991) and the present study.

Finally, Wolpert and Ghahramani (2000), Wolpert, Ghahramani, and Jordan (1995) and Miall, Weir, Wolpert, and Stein (1993) (cf. Desmurget & Grafton, 2000) have argued for "forward models" of motor control, on the basis of principles of engineering. These forward models rely heavily on an efference copy (i.e., "blueprint") of the motor plan delivered from planning to on-line control centers. Within this framework, error reduction is contrasted between the current state and planned future state of the motor system. This system would accommodate perturbations by effecting a change in the plan that is then forwarded to the execution system such that it also reacts to the perturbation.

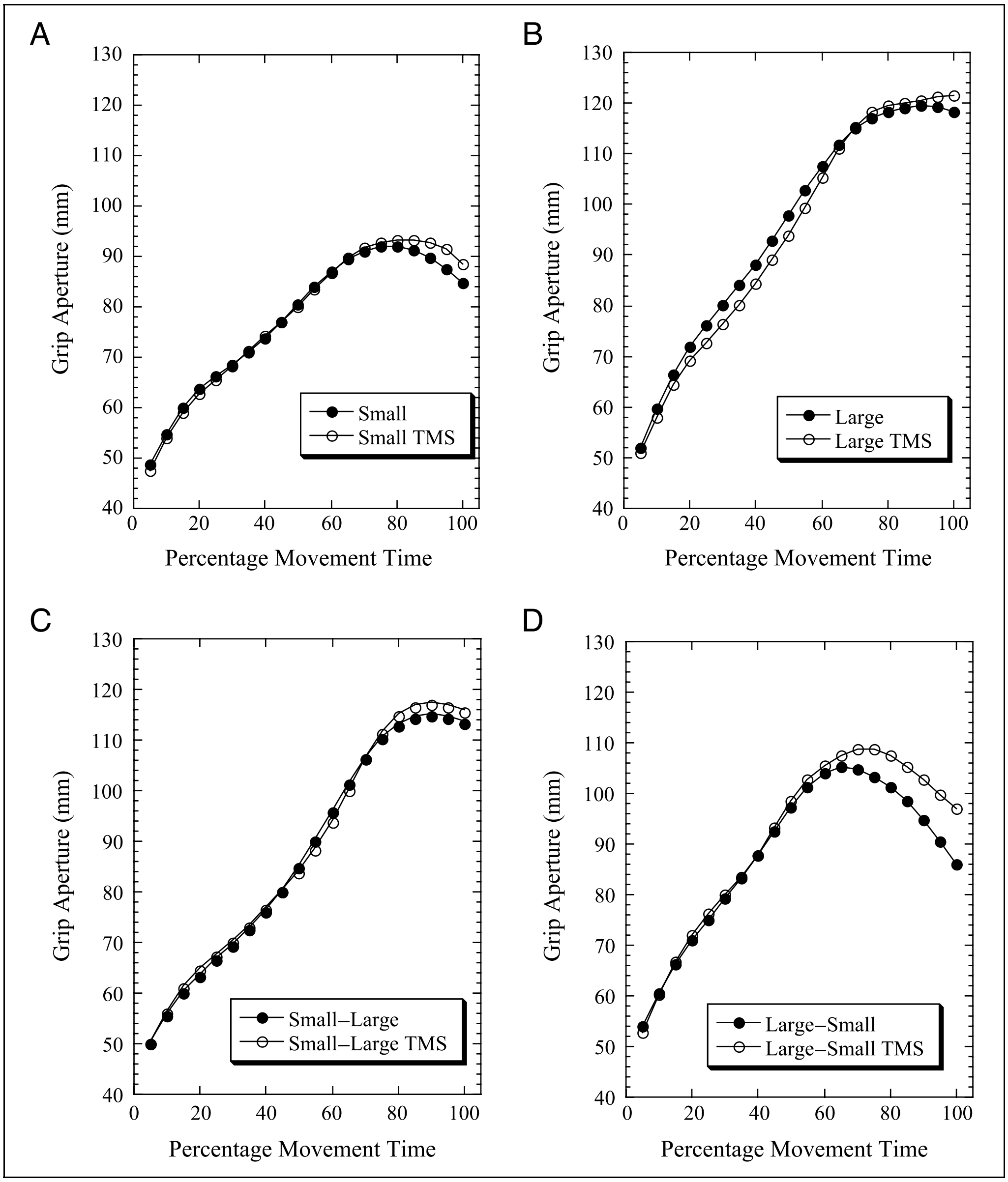
Several Stages of On-line Control

Here, we observed that stimulation of the IPS using rTMS disrupted the on-line adjustment of movements directed towards a target that had changed in size. Specifically, this disruption was particular to a coincidence between the timing of the rTMS and the *initiation* of the adjustment.

Figure 7 shows the putative stages of an on-line adjustment to a target perturbation. The most notable difference between this and previous formulations of on-line control is the division of the implementation of the on-line adjustment into an initiation and an execution stage. Whereas this is intended to address the results of the current study, it would be interesting to see in what ways the results might generalize to other perturbation paradigms, or even to movements made to constant, nonperturbed targets (such movements often exhibit small on-line corrections).

The identification of the parietal cortex with on-line adjustments to movements, and more particularly some aspect of the central processing stages shown in Figure 7, is consistent with other neurophysiological and neuropsychological results. It is known that parietal lesions, unlike premotor cortex lesions, do not impair the initial decision to act and the selection of which movement to make (Pisella et al., 2000; Rushworth, Nixon, & Passingham, 1997). Similarly, single neuron recording and fMRI studies also suggest that superior parietal activity, unlike premotor cortex activity, is not directly correlated with the selection of movements that are about to be executed (Thoenissen, Zilles, & Toni, 2002; Kalaska & Crammond, 1995).

Figure 5. Experiment 2: Grip aperture over time for each trial type, comparing control and TMS trials. (A) Small target trials; (B) Large target trials; (C) Small–Large perturbation trials; (D) Large–Small perturbation trials. Note the large effect of the TMS between 80% and 100% of movement time in the Large–Small condition (D).



Although some superior parietal cells increase their firing rates as soon as a target for reaching appears or during a preparation period prior to actually moving, such neurons are most prominent in the most caudal parts of the SPL. In contrast, there is a wide distribution throughout the lobule of activity at the time of actual movement (Johnson, Ferraina, Bianchi, & Caminiti, 1996). Although it may occur comparatively late in time during the course of the reaching movement, superior parietal neuron activity is not simply due to sensory feedback from the moving arm. The SPL also has access to an efference copy of the movement. Seal, Gross, and Biolac (1982), for example, showed that the late period activity of superior parietal neurons continues even after deafferentation by dorsal rhizotomy. The initiation of an on-line adjustment is only possible if the current state of the arm is known in addition to the target position and it is clear that such information is encoded in parietal neuron activity.

More recently, several studies have directly examined the importance of the parietal cortex when on-line adjustments are required. Desmurget, Grea, et al. (2001) reported a change in regional cerebral blood flow in the IPS when subjects were adjusting pointing movements made to a target that had jumped. Parietal disruption, either as a result of TMS or a lesion, impairs the on-line control of movements (Grea et al., 2002; Pisella et al., 2000; Desmurget, Epstein, et al., 1999). The present results, however, emphasize that on-line control does not just operate at the last stages of a movement but also operates in the first half of the movement period. Furthermore, the results show that the parietal cortex contributes to on-line control even at these early stages. Parietal TMS may also disrupt the adjustment of a

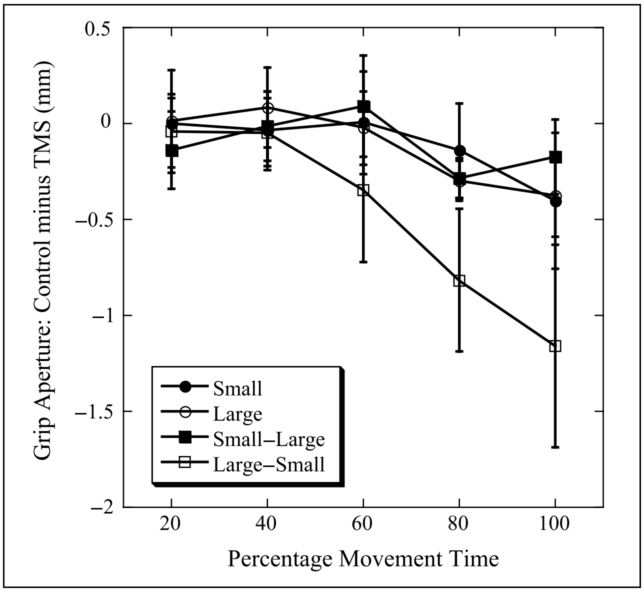


Figure 6. Experiment 2: Effects of TMS on grip aperture at each 20% of movement time for each trial type. Error bars represent standard errors of the mean.

movement away from a previously prepared plan (Rushworth, Ellison, & Walsh, 2001). Different studies have focused discussion on either the IPL or the SPL, but across experiments it is clear that the critical area consistently surrounds the IPS as in the present investigation. It is likely that more lateral regions in the IPL are concerned with distinct aspects of movement planning (Glover, 2004).

Another relevant issue is the well-known distinction between the reaching and grasping components of movement (Jeannerod, 1984). This distinction also appears to have its neural counterpart, with grasping associated with more anterior regions of the parietal lobes (Binkofski et al., 1998; Grafton et al., 1996) and reaching with more posterior regions (Connolly, Andersen, & Goodale, 2003). Thus, one must be cautious about generalizing the results of the present study of grasping to the domain of reaching. As mentioned above, a reaching–grasping distinction also may underlie the slightly different results obtained in the present study and in that of Desmurget, Epstein, et al. (1999).

Whereas the present study implicates the IPS in the initiation of the on-line adjustments of grasp to a change in target size, it cannot address the questions of what other contributions the parietal cortex may make to on-line control or how other regions of the brain are involved in other stages of the on-line process. The initial perception of a change in the target clearly requires visual processing, and the transmission of this information through the dorsal visual stream to motor areas in the parietal lobes. The parietal cortex is also known to be important when comparing internal and external feedback about hand position (Sirigu, Daprati, Pradat-Diehl, Franck, & Jeannerod, 1999). The stages between such comparison processes and the initiation of a correction are likely to involve not just the parietal cortex but also the cerebellum with which it is densely interconnected (Miall, 1998; Schmahmann & Pandya, 1989). Execution of the required adjustments would likely involve areas more closely connected to the musculature, such as the primary motor cortex.

Two facets of this account of on-line control are strongly supported by the results of the present study. First, it is clear that an initiation phase for on-line adjustments exists independently of its ultimate execution. Second, the IPS in humans would seem to provide the critical impetus for the initiation of on-line adjustments, although it may not be critically involved in the other stages of on-line control. These two main findings may open many possibilities in expanding our understanding of parietal lobe function in on-line control.

METHODS

Subjects

Six paid volunteers participated in Experiment 1. One of these six and five new subjects participated in Experi-

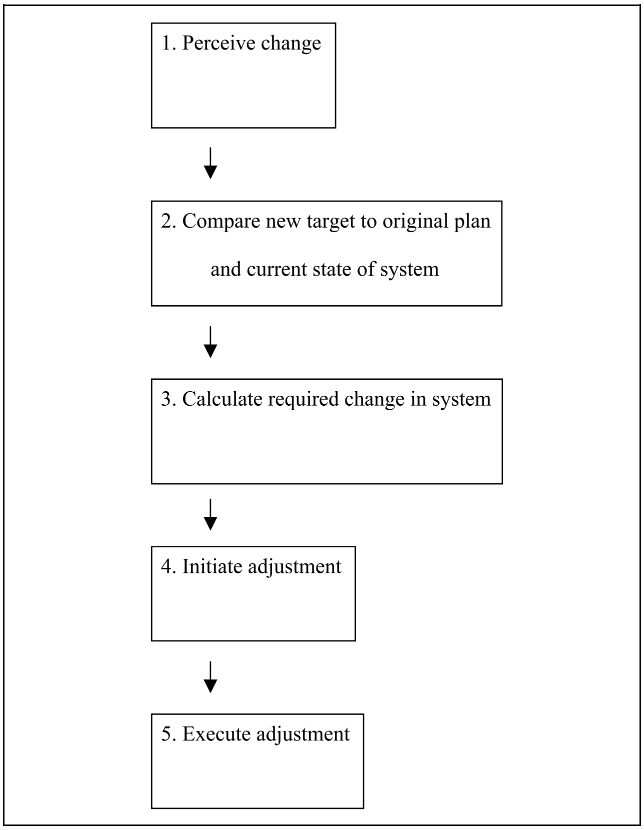


Figure 7. A schematic model of the stages involved in on-line adjustments to a change in the target. The present study suggests a role of the IPS in stage 4 (initiating the adjustment).

ment 2. All subjects had normal or corrected-to-normal vision, were right-handed by self-report, and were naive as to the exact purpose of the study. All subjects gave their informed written consent before participation. The procedures were approved by the Oxfordshire Regional Ethics Committee (OxREC no. C02.092).

Apparatus

Subjects sat at a chair in front of a solid wood 122 × 82 cm table. The subject's head was restrained using an adjustable chin rest set at a comfortable height. An 18 × 9 × 2 cm (in height) box containing a start key was fastened to the table using Velcro fasteners directly in front of the subject's midsection, such that the center of the start key was 8 cm from the edge of the table closest to the subject. The start key was 8 cm wide in the horizontal plane and 2 cm wide in the frontal plane of the subject, and protruded approximately 2 cm above the top of the box. A small (0.5 cm) circular marker was centered on the start key to serve as a starting position indicator.

The targets used were two perspex objects situated on a metal base. The large target was a hollow circular ring 6 cm in height and 6.5 cm in diameter, with 3-mm-thick edges. The small target was a solid cylinder 10 cm in height and 1.5 cm in diameter. The small target was nested in a central position inside of the large target; because of the difference in height of the two targets, the small target protruded 4 cm above the top of the large target. Both targets sat in custom holding places built into the metal base. Both targets were painted at the top and bottom with a thin strip of metallic paint, which allowed the computer to determine when contact was made or broken between either the subject's hand and the target, or the target and the metal base. The metal base was 18.5 cm in width along the subject's horizontal plane, 10.5 cm thick in the subject's depth plane, and 7 cm tall. The metal base housed LEDs that were used to light the targets from underneath, making them visible in the dark.

The positioning of the targets was such that the near and far edges of the large target were 44 and 50.5 cm, respectively, from the starting position of the subject's hand. The near and far edges of the small target were 46.5 and 48 cm, respectively, from the starting position of the subject's hand.

Procedure

The study was conducted in a darkened room. Subjects sat at the table with their head resting comfortably on the chin rest. Polhemus movement recording transmitters (see below) were attached to the subject's thumb and index fingernails. At the beginning of each trial, the subject placed their right thumb and index finger together, with the tip of the index finger on top of the circular dot on the starting key, pressing the key down. When the key was pressed, the computer emitted a low tone to signal that the trial was going ahead. At a variable 1–3 sec after this tone, the computer sent a signal to light the LEDs under either the small or large target, making that target visible. The subject's task was to reach out as quickly as possible and grasp the visible target, lifting it just enough to break contact with the metal base. Subjects were free to grasp the target with as many fingers as they wished, on the stipulation that at least the thumb and forefinger contacted the target. This was to allow for a more natural adjustment process (Castiello, Bennett, & Stelmach, 1993). On some trials (perturbation trials), the visible target was switched (by switching the lighting from the small to the large target or vice-versa) when the subject released the start key. On these trials, subjects had to then adjust their movement to grasp the newly visible target. Once the target was lifted, breaking contact with the metal base, the LEDs were extinguished. Subjects then had to replace the target and return to the starting position.

Eight possible trial types existed, on the basis of the crossing of three factors: target size (large or small), perturbation (yes or no), and rTMS (yes or no). On nonperturbation trials, the target that was initially lit (small or large) remained lit throughout the trial. On perturbation trials, the target that was lit was switched (from small-to-large or from large-to-small) coincident with the subject releasing the starting key. Of a total of 86 trials, there were 27 small and 27 large nonperturbation trials, as well as 16 small-to-large perturbation and 16 large-to-small perturbation trials. rTMS was applied on 8 of the trials in each of the 4 conditions, meaning there were a total of 32 trials with rTMS and 54 trials without rTMS. The sequence of trial type was determined randomly, with the caveat that no single trial type combination occurred more than twice in succession.

Transcranial Magnetic Stimulation

rTMS was administered by means of a Magstim (Whitland, Wales, UK) rapid high-speed stimulator and a Magstim figure-of-eight coil. The areas stimulated in each experiment are shown in Figure 8. In Experiment 1, rTMS was applied for four pulses at 10 Hz, beginning coincident with release of the start key. In Experiment 2, rTMS was applied for four pulses at 10 Hz, beginning roughly halfway through the movement. To estimate the halfway point for each subject, 20–30 practice trials were run before the main testing session, and movement times for the final 10 of these practice trials were averaged. The mean movement time during the practice trials was then halved, and on trials

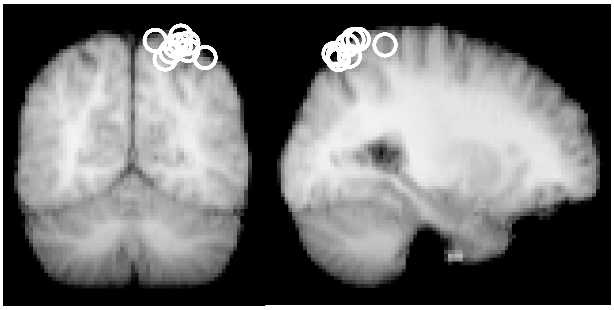


Figure 8. Gray circles indicate the position on the cortex immediately below the TMS coil on the subjects' mean MRI scan. The group mean stimulation point was at $x = -24$, $y = -59$, $z = 61$. Coronal and sagittal sections through the mean MRI scan are shown at the level of the mean stimulation point ($y = -59$ and $x = -24$, respectively) on the left and right, respectively. The left hemisphere is shown on the right of the coronal section. It can be seen that the points of maximum stimulation were, as intended, immediately adjacent to the IPS in the SPL.

when rTMS was administered, it began at this time approximately halfway through the movement. In both experiments, intensity of stimulation was set to 10% above the threshold for eliciting a visible twitch of the index finger when the TMS was applied while subjects held their hand out in a "fan" shape (subjects were instructed to dorsiflex at 10% of full force). TMS intensity was therefore set between 45% and 65% of the Magstim stimulator's maximum output. The coil was then moved and positioned over the IPS (Figure 6). A Polaris (Northern Digital, Waterloo, Canada) infrared tracking device was used to record the position of the subject's head and the TMS coil, and Brainsight software (Rogue Research, Montreal, Canada) was used to coregister the subject's head with the subject's structural MRI scan. The TMS coil was placed just (i) medial to the IPS, so that it was always over the SPL and (ii) approximately 1.5 cm posterior to the level of the superior part of the postcentral sulcus. Each subject's brain MRI was subsequently registered to an average of 305 brains aligned with Talairach space (Collins, Neelin, Peters, & Evans, 1994; Talairach & Tournoux, 1988), using Oxford Centre for Functional Magnetic Resonance Imaging of the Brain Software Library tools (FMRIB, Oxford, UK; www.fmrib.ox.ac.uk/fsl) so that it was possible to establish the stimulation coordinates in standard space. The mean TMS stimulation coordinates were at $x = -24$, $y = -59$, and $z = 61$ in standard space.

Movement Recording

A Polhemus motion analysis system was used to record three-dimensional position data from the two transmitters. The system was set up so that position data were recorded alternately from the two transmitters (i.e., 1, 2, 1, 2, etc.) at 120 Hz. This meant that each marker was recorded at 60 Hz. The raw position data were then fed into an off-line program for analysis.

Data Analysis

Data were analyzed by first passing them through a custom filter designed to reduce artifacts. The position of the transmitter that was not active at each point in time (because the recording alternated between the two markers) was estimated by linear interpolation. The onset of each movement was determined as the time from the start of the trial when the velocity of the thumb first exceeded 5 cm/sec. The offset of the movement was determined as the time from the end of the trial when the velocity of the thumb first fell below 5 cm/sec. The thumb was used for determining onset and offset thresholds as it tends to be the more stable digit in grasping (Wing, Turton, & Fraser, 1986; Wing & Fraser, 1983). For both experiments, we analyzed reaction times and movement times. Movements were then normalized into 20 equally timed intervals between movement onset and offset. Grip aperture was measured as the distance between the two markers in three-dimensional space.

We conducted three sets of planned comparisons. In each case, *t* tests were used to determine the presence or absence of a statistically significant effect. The first set of analyses compared movement times in each of the six combinations of interest (see below) to determine the validity of the normalization procedure, as time normalization assumes equal movement times across conditions of interest. The second set of analyses compared the control and perturbation trials collapsed across both experiments to determine the timing of the perturbation effects on grip. The third set examined the effects of TMS on grip in each experiment.

The perturbation comparisons tested for differences between the perturbation trials and the nonperturbation trials. Trials were compared in which the initial size of the target was the same, but in which a perturbation did or did not take place. Specifically, Small–Large trials were compared to Small trials and Large–Small trials were compared to Large trials. These comparisons involved only control (non-TMS) trials. In order to increase the power of the analysis, data from the control conditions were collapsed across experiments.

The four TMS comparisons tested for differences between the control (non-TMS) and TMS trials for each of the size and perturbation conditions (Small, Large, Small–Large, and Large–Small) at each 20% of movement time. These comparisons were conducted separately for each experiment.

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