Time Course of Determination of Movement Direction in the Reaction Time Task in Humans

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Received 9 November 2000; accepted in final form 5 June 2001

INTRODUCTION

In monkeys, cell recordings from the motor cortex have shown increased activity 200–500 ms before the onset of voluntary movement (Kubota and Hamada 1979), and a specification of movement direction 150–100 ms before the onset of voluntary movement (Georgopoulos 1995; Georgopoulos and Pellizer 1995; Georgopoulos et al. 1988, 1989). The latter result was based on simultaneous recordings from a sample of motor cortex cells. The preferred direction of each cell and its firing rate at different time points during the reaction time were analyzed to calculate a “population vector” indicating the direction signaled by all the cells acting together. It was found that the vector increased in length and rotated toward the target direction during the reaction time (RT).

Sommer, Martin, Joseph Classen, Leonardo G. Cohen, and Mark Hallett. Time course of determination of movement direction in the reaction time task in humans. J Neurophysiol 86: 1195–1201, 2001. The primary motor cortex produces motor commands that include encoding the direction of movement. Excitability of the motor cortex in the reaction time (RT) task can be assessed using transcranial magnetic stimulation (TMS). To elucidate the timing of the increase in cortical excitability and of the determination of movement direction before movement onset, we asked six right-handed, healthy subjects to either abduct or extend their right thumb after a go-signal indicated the appropriate direction. Between the go-signal and movement onset, single TMS pulses were delivered to the contralateral motor cortex. We recorded the direction of the TMS-induced thumb movement and the amplitude of motor-evoked potentials (MEPs) from the abductor pollicis brevis and extensor pollicis brevis muscles. Facilitation of MEPs from the prime mover, as early as 200 ms before the end of the reaction time, preceded facilitation of MEPs from the nonprime mover, and both preceded measurable directional change. Compared with a control condition in which no voluntary movement was required, the direction of the TMS-induced thumb movement started to change in the direction of the intended movement as early as 90 ms before the end of the RT, and maximum changes were seen shortly before the end of reaction time. Movement acceleration also increased with maxima shortly before the end of the RT. We conclude that in concentric movements a change of the movement direction encoded in the primary motor cortex occurs in the 200 ms prior to movement onset, which is as early as increased excitability itself can be detected.

METHODS

We investigated six healthy, right-handed subjects using a choice RT task. All but one subject were investigated twice to assess the intra-individual variability of the results, and each recording was analyzed as an independent data set. The protocol was approved by the institutional review board, and all subjects gave their written informed consent. None of the subjects had a history of neurological disease or any signs of visual deficits as could be determined by a routine neurological examination. The mean age was 45.2 (range 24–62) years. Handedness was determined by the Oldfield handedness questionnaire (Oldfield 1971), and subjects had more than 18 of 23 points of right-handedness. The subjects were seated in front of the screen of the computer that controlled the experiment (Macintosh Iici, Apple Inc., Cupertino, CA). The right forearm, wrist, and fingers 2–5 were supported by a holder. This holder kept the hand in a slightly extended and pronated position. In this setup, the axes of abduction/adduction and of flexion/extension were close to the horizontal and vertical space axes, respectively. During a typical trial, three successive signals occurred on the screen: a warning stimulus of 1,000 ms duration, a go-signal of 10 ms duration indicating the requested direction of movement, and a blank signal of 8,000 ms duration (Fig. 1). We administered two types of go-signals in a pseudorandom order: One was an arrow to the left, thus requesting thumb extension, i.e., when viewed from behind, a movement in the 9 o’clock direction (9:00 task). The other one was a downward arrow, indicating thumb abduction, i.e., a movement in the 6 o’clock direction (6:00 task). The subjects were asked to relax completely before trial onset and to move

In humans, evidence for increased motor cortex excitability during the RT has been provided by transcranial magnetic stimulation (TMS) (Pascual-Leone et al. 1994; Tomberg 1995). TMS can also indicate the directional excitability of a stimulated region of the motor cortex (Classen et al. 1998). Development of directional specificity during the reaction time was shown by Ghez and colleagues from studies in which subjects were forced to move before completing full movement planning (Ghez et al. 1997).

Using TMS, we sought to determine 1) the timing of the premovement specification of movement direction in the human motor cortex and 2) how its time course relates to that of motor cortex facilitation, i.e., whether the specification of movement direction occurs simultaneous with or after increased motor cortex excitability.

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their right thumb briskly in the requested direction immediately after
the go-signal occurred on the screen. Acoustic feedback of the
electromyographic (EMG) signal was provided throughout the experiment
to ensure complete relaxation during each trial.

Trials of five experimental conditions were presented in a random-
ized order. In condition 1, the 9:00 go-signal was combined with single TMS
to determine the RT individually as well as the movement direction in
the 9:00 task. In condition 2, the 6:00 go-signal was investigated
without TMS to find similar baseline data. In condition 3, TMS
stimuli were presented with no preceding go-signal. This made it
possible to determine the baseline motor-evoked potential (MEP) as
well as the direction of the involuntary thumb movement evoked by
TMS. To keep the subjects’ attention comparable with the other
conditions, the usual warning stimulus was presented; it ended 10 ms
before the TMS stimulus. In condition 4, the 9:00 go-signal was
combined with single TMS at various delays. This allowed determi-
ation of the amplitude of the MEP as well as the direction of thumb
movement at various intervals before onset of the 9:00 movement. In
condition 5, the 6:00 go-signal was combined with single TMS at
various delays. This allowed determination of the amplitude of the
MEP as well as the direction of thumb movement at various intervals
before onset of the 6:00 movement. Each experiment consisted of 20
trials with TMS only, 20 trials without TMS (10 each for the 6:00 and
9:00 movements), and the remaining 120 were equally distributed
among the 6:00 and the 9:00 tasks, with 10 trials for each of the
selected intervals between go-signal and TMS. These intervals were
adjusted so as to cover the time window of 200 ms before the end of
the individual RT that had been determined in 40 practice trials
undertaken before starting the actual experiment. The different condi-
tions were pseudorandomly administered; inter-trial interval was
8 s.

Magnetic stimulation was delivered from a Cadwell high-speed
magnetic stimulator (Cadwell Labs, Kennewick, WA) and adminis-
tered via a figure eight–shaped coil in which the outer diameter of
each wing was 55 mm. The coil was placed over the left motor cortex
at the optimal position evoking isolated thumb movements of the right
hand. Before starting the actual experiment, we determined the min-
imal intensity of stimulation capable of inducing slight thumb move-
ments visible to the experimenter’s observation in at least 5 of 10
trials. The average movement threshold across subjects was 56%
(range 45–62%) of the maximum stimulator output. Intensity of
stimulation was 10% above the individual movement threshold. In a
typical trial, a single magnetic stimulus was triggered by the computer
that controlled the experiment at delays varying from 10 to 280 ms
after occurrence of the go-signal.

TMS-evoked movements were recorded at 3,000 Hz sampling
frequency by two EMG channels and two accelerometers. For the
EMG, surface electrodes were fixed with adhesive tape over the
abductor pollicis brevis (APB), which is mainly involved in the 6:00
downward movement, and over the extensor pollicis brevis (EPB,
9:00 movement). The signals were amplified by a Counterpoint EMG

FIG. 1. Order of stimuli and events per trial.
device (Dantec, Skovlunde, DK), low-pass filtered at 100 Hz, depicted on the EMG screen for visual control, and transferred to a data-storing PC (Premium 386/33, AST Research, Taiwan). The EMG data provided information about the RT between the go-signal and the onset of voluntary movement as well as about the amplitude of the MEP. Two accelerometers (Picotrax, Endevco, San Juan Capistrano, CA) were fixed on the radial side of the proximal thumb phalanx. One of them was oriented in the axis of abduction and adduction, the other in the axis of flexion/extension; both were equally calibrated in units of millivolt/g. Their data were amplified with a gain of 100 (40 dB, device built by the Research Services Branch, NIH, Bethesda, MD), filtered between 0.4 and 100 Hz, displayed on the EMG screen for visual control, and transferred to the data-storing PC. A control experiment showed that the first peak of accelerometer data (Classen et al. 1998) provides sensitive information about the direction of thumb movements (Fig. 2A; for details see legend). We assumed that accelerometers are superior to tracking devices in detecting minimal displacements of the thumb frequently induced by TMS at weak intensities.

**Data analysis**

In a typical trial, two bursts of EMG activity were observed: one sharp and short potential reflecting the involuntary movement evoked by the transcranial stimulus and a second large and broad potential reflecting the voluntary activity in response to the go-signal. These two bursts of EMG activity were accompanied by two separate shifts in the accelerometer traces. A typical example of the raw data of one trial is shown in Fig. 2B. Trials in which there was background activity with amplitude of more than 25 μV in the first 100 ms of recording were rejected from analysis.

Since TMS may influence the RT (Day et al. 1989), we determined the RT in trials without TMS and measured the latency of the onset of the broad peak of voluntary EMG activity. The RT of the APB was used for the task that involved abduction more than extension (6:00); for the 9:00 task we used the RT of the EPB.

**Statistical procedures**

In each trial with go-signal and TMS, we subtracted the delay between the go-signal and the MEP from the individual average RT of the appropriate muscle (APB for the 6:00 task, EPB for the 9:00 task) as determined in the TMS-free trials. The resulting latency indicated when, during the RT, an MEP had occurred. To reveal the time course of MEP amplitudes, the movement direction and the acceleration of TMS-induced thumb movements, we subdivided the RT into bins. To keep the number of samples per bin similar, the bins earlier than 150 ms before the end of the RT were 50 ms wide, and those later than 150 ms before the end of the RT were 30 ms wide, since fewer trials were recorded with TMS early rather than late in the RT.

In each trial, movement direction was determined as an angle calculated from the arctangents of the first peak acceleration. In trials with TMS only, this enabled determination of the baseline movement direction; in trials with a go-signal and TMS we could determine the direction of movement during the RT. In trials without TMS, we calculated the individual target direction from the first voluntarily induced peak of each accelerometer recording. In both situations, we performed a trigonometric averaging of movement angles (see APPENDIX) of trials corresponding both in task and delay from the go-signal. In each subject, we calculated the deviation (in deg out of 360°) between the average baseline direction and the average target direction for either task. Similarly, we determined the deviation of TMS-induced movement directions from the target direction of the corresponding task (in deg) and normalized it to the baseline deviation. In each subject, we averaged the deviations from target with the same latency before the end of the RT. In addition, the nonaveraged movement directions were analyzed with circular statistics using the Watson U²-test (Batschelet 1981). We compared the individual baseline and target directions for either task, and the movement directions obtained earlier with those obtained later than 100 ms before the end of RT.

In these analyses, the null hypothesis was that the two sets of data do not differ significantly from each other in terms of movement direction. Also, we determined the mean angular deviation as a measure of variability of movement directions (Batschelet 1981). To detect whether the amplitude of the first peak of acceleration changes during the RT, we calculated the length of the vector resulting from the first peaks of acceleration measured by either accelerometer. MEP amplitudes of TMS-induced thumb movements were measured off-line as peak-to-peak amplitudes from APB and EPB. Data were normalized to the individual baseline MEP amplitude that was determined in the trials with TMS, but without go-stimulus.

To compare the time courses of prime mover and nonprime mover, we calculated a repeated measures ANOVA with the internal factors bin and parameter (i.e., normalized MEP amplitude of prime- or nonprime mover, values of both tasks pooled for either parameter).

To determine which bins of averaged movement directions, first peak accelerations and normalized MEPs differed from baseline, we used noncorrected t-tests (Perneger 1998). All data are indicated as mean values ± standard error.

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**TABLE 1. Baseline and target directions**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Experiment</th>
<th>Baseline (deg)</th>
<th>AD</th>
<th>Target 6:00 (deg)</th>
<th>AD</th>
<th>Target 9:00 (deg)</th>
<th>AD</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>26.25</td>
<td>75.10</td>
<td>305.86</td>
<td>10.35</td>
<td>179.25</td>
<td>26.04</td>
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<td>1</td>
<td>2</td>
<td>68.47</td>
<td>75.76</td>
<td>295.70</td>
<td>8.93</td>
<td>181.17</td>
<td>32.72</td>
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<tr>
<td>2</td>
<td>1</td>
<td>39.16</td>
<td>31.14</td>
<td>294.57</td>
<td>34.67</td>
<td>161.85</td>
<td>60.60</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>31.13</td>
<td>35.48</td>
<td>271.11</td>
<td>19.23</td>
<td>188.65</td>
<td>61.96</td>
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<tr>
<td>3</td>
<td>1</td>
<td>145.84</td>
<td>37.10</td>
<td>263.19</td>
<td>12.64</td>
<td>183.38</td>
<td>52.40</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>148.63</td>
<td>27.19</td>
<td>281.02</td>
<td>10.99</td>
<td>204.53</td>
<td>44.55</td>
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<tr>
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<td>1</td>
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<td>74.21</td>
<td>276.71</td>
<td>31.97</td>
<td>156.47</td>
<td>7.76</td>
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<tr>
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<td>181.91</td>
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<tr>
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<td>44.90</td>
<td>292.94</td>
<td>7.04</td>
<td>154.06</td>
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<tr>
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<td>1</td>
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<td>21.80</td>
<td>282.09</td>
<td>44.77</td>
<td>196.73</td>
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<tr>
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<td>276.43</td>
<td>42.75</td>
<td>205.81</td>
<td>36.65</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>65.34</td>
<td>64.52</td>
<td>284.26</td>
<td>16.57</td>
<td>181.31</td>
<td>23.61</td>
</tr>
</tbody>
</table>

Values in Baseline, AD, and Target are expressed in deg. Baseline directions recorded in trials in which only transcranial magnetic stimulation (TMS) was presented in the absence of voluntary movement, and target directions reflecting the performance to aim at the target in trials without TMS. All subjects except subject 5 participated in 2 identical experiments. Directions are indicated as angles on a circle ranging from 0° to 360° as specified in Fig. 2D. AD, angular deviation.
RESULTS

Reaction time (RT)

In the trials without TMS, the average onset of voluntary EMG activity in the APB muscle was 304 ± 6 ms in the 6:00 task and 298 ± 4 ms in the 9:00 task (t-test, nonsignificant). The average onset of voluntary EMG activity in the EPB muscle was 307 ± 4 ms in the 6:00 task and differed significantly from the onset in the 9:00 task (289 ± 4 ms, t-test).

In trials with TMS, RTs were significantly prolonged. The average RT of the APB muscle was 320 ± 2 ms in the 6:00 task and 312 ± 2 ms in the 9:00 task. The difference between the tasks was significant. For the EPB muscle, average RTs were 326 ± 2 ms in the 6:00 task and 305 ± 2 ms in the 9:00 task. Again, there was a significant difference between tasks.

Simple regression analyses relating RT and the chronological number of the trial did not yield any significant change in RT during the course of the experiment in any subject for any of the investigated muscles, indicating the absence of learning.

Angle of TMS-induced thumb movement

Individual baseline directions as determined in TMS-alone trials and individual target directions are shown in Table 1. In each subject, the directions were consistent with the theoretical directions: the 9:00 task showing a larger variation of target directions than the 6:00 task. Baseline and target directions were generally similar in two successive experimental sessions in the same subject, the overall variability of baseline directions being larger than that of the target directions. Circular statistics (Watson U²-test) confirmed a significant difference between baseline and target directions in both tasks.

In each subject, TMS-induced movement directions during the RT shifted from baseline direction toward target direction of either task. Hence, the difference between actual movement direction and target direction decreased during the RT. A typical example is shown in Fig. 3. Across subjects, the first bin that was significantly closer to the target than the baseline occurred 61–90 ms before the end of the RT in the 6:00 task.
and 1–30 ms in the 9:00 task (t-tests). The shift of directions was more complete in the 6:00 task than in the 9:00 task. Circular statistics across subjects confirmed a change of TMS-induced movement direction during the RT for both tasks (Table 1, Fig. 4C). During the RT, the angular deviation increased in subjects 2 (trial 2), 3 (both trials), and 6 (trial 2), it decreased in subject 4 (both trials), and remained essentially unchanged in all other trials and subjects.

**Motor evoked potentials**

Across tasks and muscles, we found a significant interaction of muscle × task (repeated-measures ANOVA, $F = 35.0, P < 0.0001$), confirming the hypothesized task-related predominance of the appropriate muscle. There was neither a significant effect of muscle nor a significant effect of task, ruling out a nonspecific predominance of either muscle or task.

The time courses of the prime mover (APB in 6:00 task, EPB in 9:00 task) and the nonprime mover differed from each other (effect of parameter, $F = 42.2, P = 0.007$) because the facilitation of the prime mover occurred earlier (post hoc t-test, 151–200 ms) than the facilitation of the nonprime mover (91–120 ms, Fig. 4, A and B).

**Acceleration of MEP-induced thumb movement**

There was a trend for increasingly accelerated TMS-induced movements during the course of the RT. The first bin that yielded a significant difference from baseline occurred 61–90 ms before the end of the RT in either task (Fig. 4D).

**Discussion**

Our results provide evidence for an involvement of the human motor cortex in a selective prime mover facilitation of muscles acting on the same joint and, as a result of prime mover facilitation, in a specification of movement direction. We show that the facilitation of the prime mover precedes a less pronounced facilitation of the nonprime mover, and that this is the most sensitive measure of direction specification. The selective facilitation of movement agonists is consistent with an earlier study (Tomberg 1995) that showed such selective facilitation in two extensors of the index [extensor digitorum (ED) and extensor indicis (EI)]. Looking at one time point relatively late in the RT of a simple RT task, the author found a facilitation of ED when an extension of fingers 2 to 5 was requested, but a facilitation of EI when only an extension of the index was requested. Our findings extend Tomberg’s data in that two muscles acting on a single joint were studied in the present paper (as well as exploring the full time course).

With conditioning-test paired pulse TMS, a recent study has shown reduced activity of intracortical inhibition during movement preparation (Reynolds and Ashby 1999). Inhibition was only reduced in the movement agonist (hand extensors), but not in the antagonist (hand flexors). This underlines the cortical origin of the selective agonist facilitation.

Determining movement direction has been studied by Ghez et al. (1997). These authors investigated a two-choice RT task in which subjects were forced to move before the end of their ordinary RT, i.e., before the end of full movement planning. As a parameter for the degree of planning, they used the directional correctness of movements. For early parts of movement planning (forced movement times shorter than 80 ms after the go-signal), they found no directional specificity of movements. For later parts of planning (forced movement times ranging from 81 to 200 ms), there was a trend to increase correctness of movements; with forced movement times longer than 200 ms after the go-signal, the proportion of correctly directed movements sharply increased. Findings from their study are consistent with ours in that the first sign of directional specification was approximately 100 ms after the go signal (increase of the excitability of the prime mover 200 ms before the end of the reaction time with a total reaction time of about 300 ms).

In primate studies (Georgopoulos and Pellizer 1995; Georgopoulos et al. 1989), the authors investigated choice RT tasks in monkeys and described a gradual build-up of the “population vector” as calculated over a sample of single-cell recordings. The authors concluded that in movement preparation of primate, the primary motor cortex is involved in processing the motor program. This population vector change in response to a visual target was observed within 150 to 100 ms before movement onset; this time window is similar to our data regarding specification of movement direction in humans. Consistent with this, Gold and Shadlen provided evidence for a gradual determination of the direction of a forthcoming eye movement by microstimulating the monkey’s frontal eye field (Gold and Shadlen 2000).

In both tasks of our study, significant facilitation of muscles occurred earlier than the significant shift in the direction of evoked movements. Pooling the tasks confirmed that facilitation of the prime mover preceded the directional change. We conclude that the rise in excitability anticipates the directional change detected with the methods employed here and hypothesize that a certain level of facilitation of the predominant muscle is necessary to generate a kinematic change. In addition, the prime mover facilitation was more pronounced and preceded that of the nonprime mover. This points to a very early and economical way to facilitate muscles acting on the same joint, at least for the concentric movements studied here. This suggests a relative inhibition of competing motor programs (Mink 1996), even at early stages of motor planning.

In conclusion, our data expand evidence for a specific motor cortex facilitation of muscles acting on the same joint. They demonstrate that in the preparatory phase of voluntary movement this increased excitability of the predominant muscle precedes that of the nonpredominant muscle and results in a gradual change of movement direction encoded within the human motor cortex.

**Appendix**

The direction of movement was determined in each trial as an angle calculated from arctangents of the first peak accelerations. The formula is as follows: for acc1 > 0: $m = \arctan \text{acc1}/\text{acc2}$; for acc1 < 0: $m = \pi + (\arctan \text{acc1}/\text{acc2})$. There are two undefined cases, acc2 = 0 and acc1 < 0 is defined as 270°, acc2 = 0 and acc1 > 0 is defined as 90°. If the resulting value is negative, add $2\pi$. For angular transformation divide by $\pi \times 180$. To conform the resulting angle to the usual coordinate system as depicted in Fig. 2D, 90° was subtracted from all angles. The trigonometric average movement direction across a sample of trials was calculated following the formula: for $c > 0$: $m = \arctan s/c$; for $c < 0$: $m = \pi + (\arctan s/c)$, where $m$ is the average
movement direction, $s$ is the arithmetical average of the sine of each trial, $c$ is the arithmetical average of the cosine of each trial, and $\pi = 3.142$.

The authors appreciate the skillful editing of D. G. Schoenberg, M.Sc. M. Sommer was supported in part by the German Academic Exchange Service (DAAD); J. Classen was supported by the Deutsche Forschungsgemeinschaft (DFG Grant Cl 95/2-2).

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