Motor Cortical Activity during Interception of Moving Targets

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Abstract

■ The single-unit activity of 831 cells was recorded in the arm area of the motor cortex of two monkeys while the monkeys intercepted a moving visual stimulus (interception task) or remained immobile during presentation of the same moving stimulus (no-go task). The moving target traveled on an oblique path from either lower corner of a screen toward the vertical meridian, and its movement time (0.5, 1.0, or 1.5 sec) and velocity profile (accelerating, decelerating, or constant velocity) were pseudorandomly varied. The moving target had to be intercepted within 130 msec of target arrival at an interception point. By comparing motor cortical activity at the single-neuron and population levels between the interception and no-go tasks, we tested whether information about parameters of moving target is represented in the primary motor cortex to generate appropriate motor responses. A substantial number of neurons displayed modulation of their activity during the no-go task, and this activity was often affected by the stimulus parameters. These results suggest a role of motor cortex in specifying the timing of movement initiation based on information about target motion. In addition, there was a lack of systematic relation between the onset times of neural activity in the interception and no-go tasks, suggesting that processing of information concerning target motion and generation of hand movement occurs in parallel. Finally, the activity in the most motor cortical neurons was modulated according to an estimate of the time-to-target interception, raising the possibility that time-to-interception may be coded in the motor cortical activity. ■

INTRODUCTION

Studies of the neural mechanisms underlying reaching movements have been traditionally concerned with movements towards stationary targets. This approach has proved very useful for studying spatial characteristics, joint coordination, and muscle activation patterns of the reaching movements and their neural substrates, but has not addressed the more dynamic situation in which the timing and scaling of the movement have to be controlled within the context of changing visual information, e.g., to intercept or catch a moving target. The results of previous behavioral studies have shown that under these conditions, the characteristics of stimulus motion have a profound effect on the initiation as well as on qualitative and quantitative aspects of the intercepting movement (Lee, Port, & Georgopoulos, 1997; Port, Lee, Dassonville, & Georgopoulos, 1997; van Donkelaar, Lee, & Gellman, 1992). Therefore, this experimental paradigm provides dynamic interactions between visual input and movement and a fertile ground for exploring the neural mechanisms underlying successful target interceptions.

In our previous studies (Lee et al., 1997; Port et al., 1997), human subjects intercepted a moving target with a feedback cursor controlled by their hand movements. Target motion was manipulated by varying target acceleration and the interval between target onset and its arrival at the interception point, referred to as target motion time (TMT). In determining the time of movement initiation (i.e., reaction time) in this task, at least two alternative behavioral strategies can be used. One strategy would be to initiate the movement as the distance traveled by the target exceeds a certain threshold (referred to as threshold distance; Collewijn, 1972). Another would be to initiate the movement when a first-order estimate of time-to-target arrival (referred to as "τ" (τ); Lee, 1976) reaches a certain threshold value. Our previous studies showed that different subjects display different biases toward one or the other strategy (Port et al., 1997).

The brain mechanisms underlying the successful interception of a moving target should take into account both visual information about the moving stimulus and motor information regarding the limb. These types of information, and, consequently, the process of interception, should engage various visual and motor structures in the brain; e.g., areas related to the coding of visual motion, such as the middle temporal area, areas related to the planning and execution of limb movements, such as the motor cortex, and probably a host of other interconnected areas in posterior parietal and premotor cortex (see Wise, Boussaoud, Johnson, & Caminiti,

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1997). The present studies were focused on the role of the motor cortex in target interception. In this article we describe the behavioral tasks used and the results of conventional statistical analyses performed on behavioral, neural, and electromyographic (EMG) data. In the companion article (Lee, Port, Kruse, & Georgopoulos, 2001), we describe the results of a detailed analysis of the time course of cell activity and their clustering with respect to task variables. Preliminary results have been reported (Port, Lee, Kruse, & Georgopoulos, 1996).

RESULTS

Individual Differences in Behavioral Strategies

Two monkeys (Monkeys 1 and 2) were trained in a standard center-out reaching task and an interception task in which they were required to intercept a moving target at a predetermined location (Figure 1; see Methods). Two important aspects of target motion manipulated in the interception task were target acceleration and the interval between target onset and its arrival at the interception point, referred to as TMT. In both animals, the main effects of TMT and target acceleration type on the response time and their interaction were all statistically significant (repeated measures analysis of variance (ANOVA), $p < .05$). However, the two monkeys examined in the present study displayed different behavioral strategies. In Monkey 1, initiation of the movement was progressively delayed with increasing TMT. In addition, for a given TMT, response times were shorter for the deceleration conditions, than for the acceleration or constant velocity conditions. In Monkey 1, single-unit recording was performed in two separate recording sessions. Whereas eye movements were not controlled in the first recording session (referred to as Monkey 1a), the animal was required to maintain fixation on the first target throughout the trial in the second recording session (Monkey 1b). Despite this difference in the oculomotor control, the pattern of reaction times remained stable in this animal (Figure 2). In Monkey 2, response times were relatively constant regardless of TMT or target acceleration type (Figure 2).

In our previous study (Port et al., 1997), response time data in the interception task were described in terms of two different models. A threshold distance model assumes that the interceptive movement is initiated after the distance traveled by the target after its appearance reaches a certain threshold value, whereas a threshold τ model assumes that such decision is based on the first-order estimate of time-to-target's arrival at the interception point. Both of these models were fit to the response time data obtained from each recording session (Table 1). The threshold τ model resulted in a better fit for the data obtained from both recording sessions in Monkey 1, whereas the threshold distance model produced a better fit in Monkey 2. The fact that the model produced negative processing time for the threshold distance model in Monkey 1 implies that this model failed to capture even the qualitative aspects of the data (Port et al., 1997).

Population Activity in the Interception and No-Go Tasks

The spike activity of 831 active neurons was available for the analysis (407 from Monkey 1a, 197 from Monkey 1b, and 227 from Monkey 2). All of these neurons were localized in the primary motor cortex by the locations of electrode penetrations. Of these neurons, 397 cells (181 from Monkey 1b and 216 from Monkey 2) were examined during performance of both interception and no-go tasks. Except for the behavior of the feedback cursor, the visual stimuli were identical in these two tasks, but the generation of movement was required only in the interception task. This was reflected by the absence of modulation in the EMG activity during the no-go task (Figure 3). Similarly, population activity in the primary motor cortex differed substantially between these two tasks (Figure 4). Unlike the EMG activity, however, there was still a substantial amount of activity in the motor cortex during the no-go task, which was most pronounced in the conditions with 0.5 sec TMT (permutation test, $p < .001$; Figure 4). Under these conditions, activity was largest for the constant deceleration condition and smallest for the constant acceleration condition, suggesting that activity in the no-go task was

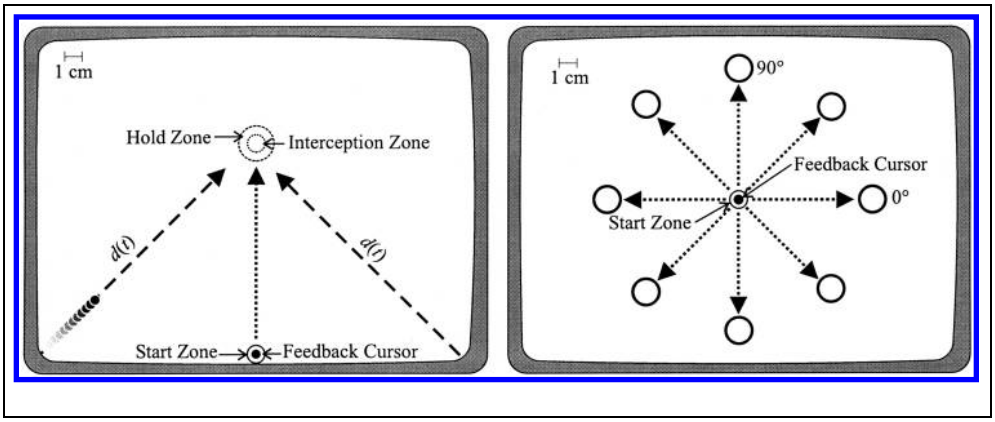

Figure 1. Behavioral task. Left: interception task. Right: center-out task.

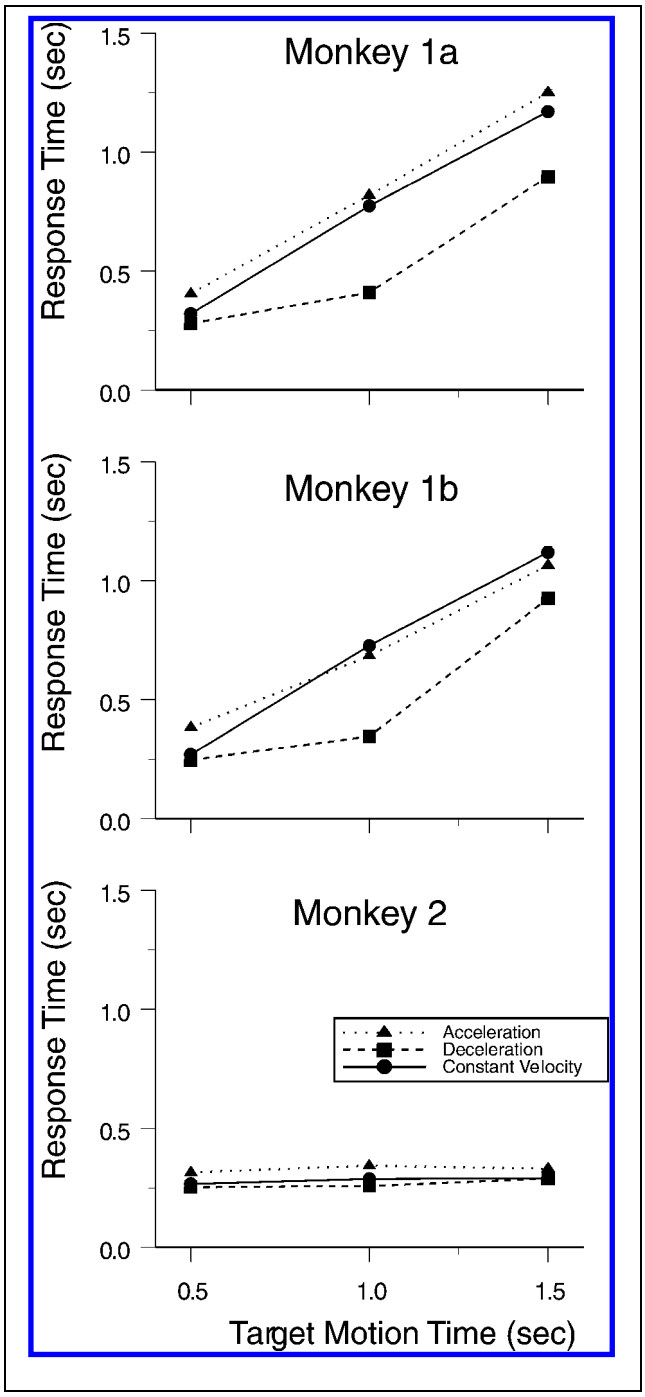

Figure 2. Effects of target acceleration type and TMT on the mean response times. Data are presented separately for different recording sessions (Monkeys 1a, 1b, and 2). Error bars (smaller than the symbols in most cases) represent *SE*.

modulated by the initial target velocity. It is also noteworthy that under the same target conditions, the profile of population activity during the interception task was similar to the activity during the no-go task throughout the period of target motion. Finally, the difference in population activity between these two tasks was larger in Monkey 2 than in Monkey 1b. This could be due to a number of reasons including the differences in the experimental design and the requirement for oculomotor fixation in Monkey 1b (see Methods).

Effects of Target Parameters on Neural Activity

A cell was deemed to be related to a particular task using the statistical criteria described in the Methods section. The overwhelming majority of cells (94%) showed statistically significant changes in activity in the no-go task, and most cells (93.3%) showed such changes in both the interception and the no-go tasks (e.g., Figure 5); only a small percentage (5.8%) of cells showed an effect only in the interception task without an effect in the no-go task (e.g., Figure 6). Furthermore, activity of many neurons was influenced by the stimulus parameters (direction of motion, motion type, and TMT) in both tasks. For each neuron, it was tested whether there were significant changes in an ANCOVA with the three stimulus parameters as repeated factors and the activity during the last 0.5 sec of start–hold time as a trial-by-trial covariate (see Methods). This last term was included because cell activity during the task may depend on its activity during the preceding start–hold period. Seven statistical terms were evaluated for each neuron, including 3 main effects (direction of motion, D; acceleration type, A; and TMT, T), 3 two-way interactions (D × A, D × T, A × T), and 1 three-way interaction (D × A × T). The results of this analysis indicated that statistically significant effects were found in a substantial number of neurons for all of these terms (Table 2). It is difficult to determine if these effects of target parameters on motor cortical activity are directly related to target parameters, because there were systematic differences in interception movement across different target conditions (Figure 2). The effects found for no-go task, in contrast, clearly demonstrated systematic effects of target parameters on motor cortical activity without any confounding effects of movement.

Comparison of Onset Times Between Interception and No-Go Tasks

Differences in the response time data between the two animals described above were reflected in the distributions of onset times for neural activity in the intercep-

Table 1. Parameters From the Threshold Distance and Threshold τ Models

	Threshold Distance Model			*Threshold τ Model*		
	PT	*TD*	R^2	*PT*	*TT*	R^2
Monkey 1a	−0.04	13.09	.75	0.24	0.53	.85
Monkey 1b	−0.14	14.55	.63	0.26	0.49	.79
Monkey 2	0.26	0.30	.11	0.30	4.0	.09

PT = processing time (sec); TD = threshold distance (cm); TT = threshold τ.

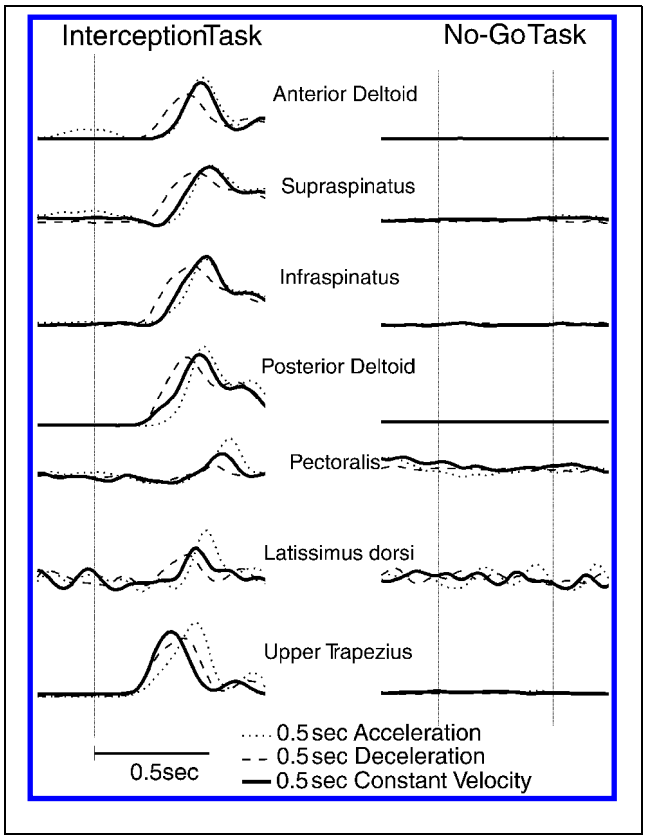

Figure 3. Comparison of EMG activity between the interception and no-go tasks. These data were obtained from 0.5-sec TMT conditions. Two vertical lines in each task represent the time of target onset and target arrival at the center of interception zone, respectively.

tion task (Figure 7). In Monkey 1b, cumulative probability histograms for onset times show that there are two separate clusters of onset times that are tightly related to target and movement onset, respectively (Figure 7, top). This separation was revealed because of the systematic changes in the response time across different target conditions. On the other hand, in Monkey 2, the distributions of onset times were similar across all target conditions (Figure 7, bottom), consistent with the fact that in this animal, the response time was relatively unaffected by the target parameters (Figure 2).

Onset times of neural activity in the no-go task were also systematically affected by the TMT (Table 3; Figure 8). In both animals, the mean onset time increased with the TMT. In addition, there was a tendency for onset times to be larger for constant acceleration and constant velocity conditions than for constant deceleration conditions. In other words, onset times were related to the initial velocity of the target. Effects of both TMT and target acceleration type were statistically significant (ANOVA, $p < .001$). In addition, these onset times of interception and no-go tasks were weakly correlated ($r = .1163$, $n = 1878$, $p < .0001$). Significant positive correlation in the onset time between the two tasks was found even when the data from the two monkeys were considered separately ($r = .1501$ and $.1099$, $n = 617$ and 1161, for Monkeys 1b and 2, respectively, $p < .001$ for both animals).

Representation of Time-to-Interception in Motor Cortical Activity

The interception task requires that the hand approach the interception task in such a way that its time to

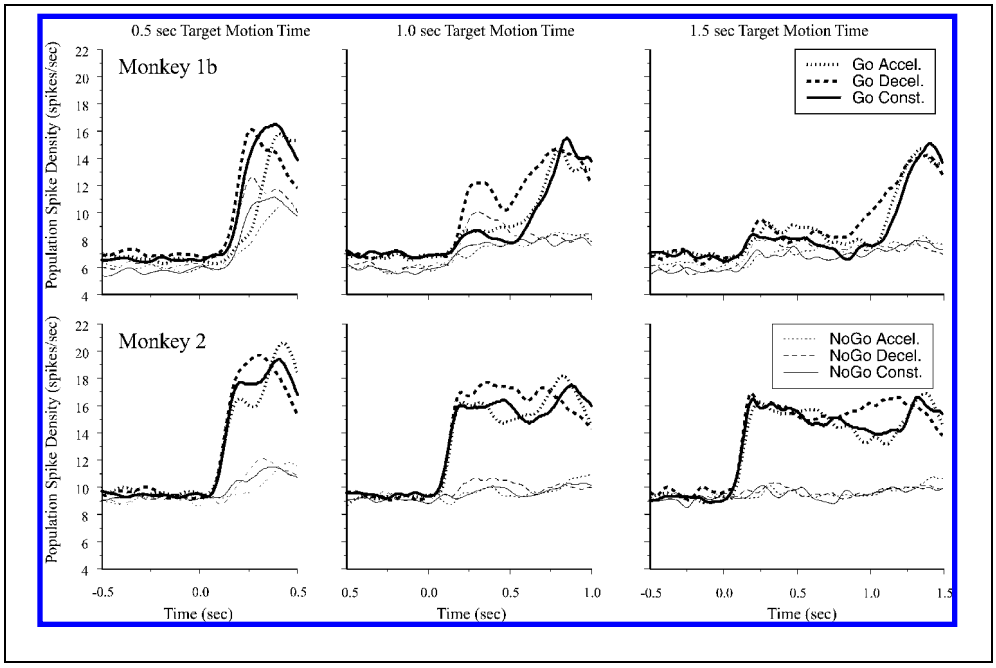

Figure 4. Comparison of population spike density functions between the interception and no-go tasks.

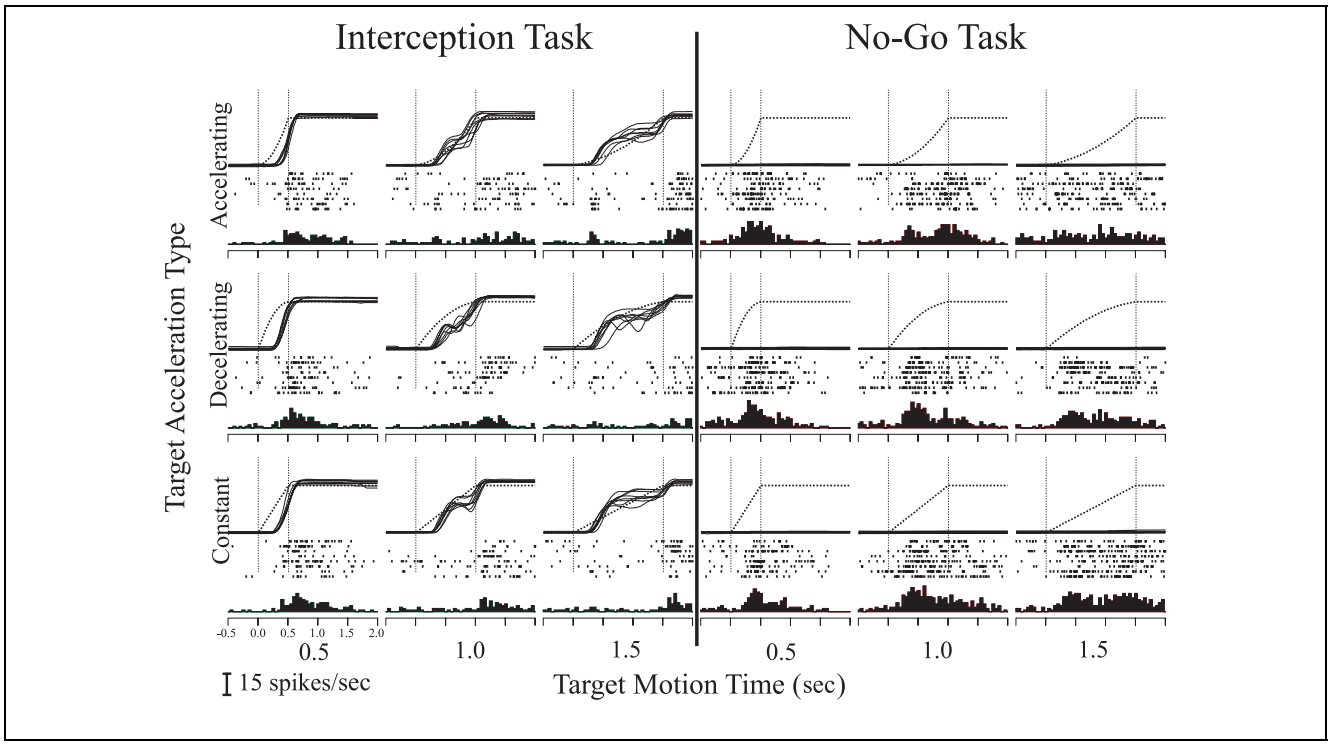

Figure 5. A neuron that was active in both interception and no-go tasks. For each combination of target acceleration type and TMT, target (dotted line) and hand (continuous line) positions along the *y*-axis (top), raster display for spike activity (middle), and peristimulus histograms (bottom) are shown. Two vertical dotted lines in each panel represent the time of the target onset and the target arrival at the center of interception zone. This neuron was more active during the no-go task than during the interception task, although this was not true in general.

arrival in the interception zone is approximately equal to the time left for the target to arrive in the same area. To examine the possibility that information about the time left for the hand to reach its destination is represented in the motor cortical activity, we applied a multiple linear regression model (see Meth-

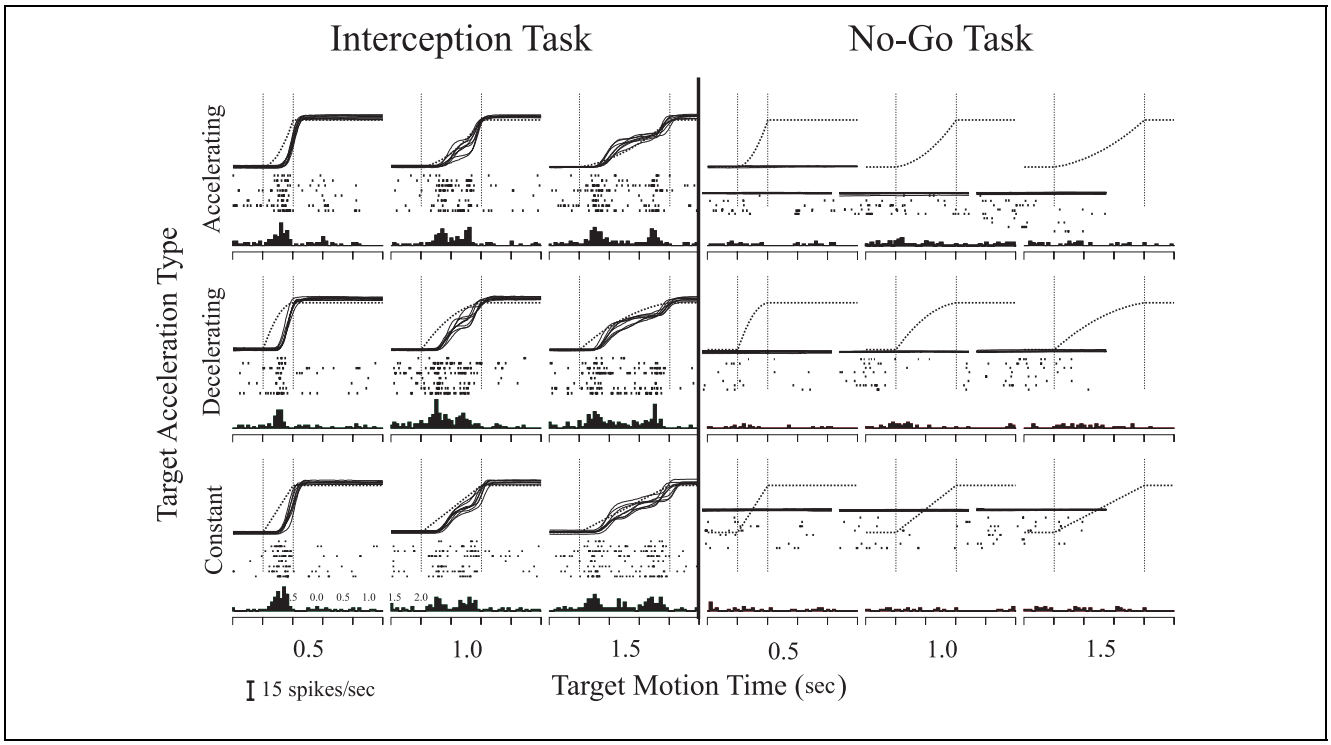

Figure 6. A neuron that was active only in the interception task. The same convention as in Figure 5.

Table 2. Number of Neurons in Which Effects of Target Parameters Were Statistically Significant for Interception and No-Go Tasks (ANCOVA, $p < .05$)

	D	*A*	*T*	*D* × *A*	*D* × *T*	*A* × *T*	*D* × *A* × *T*	*Total*
Monkey 1b								
Interception (%)	21 (12)	79 (44)	114 (63)	35 (19)	42 (23)	82 (45)	79 (44)	181 (100)
No-go (%)	17 (9)	44 (24)	84 (46)	34 (19)	33 (18)	49 (27)	50 (28)	181 (100)
Monkey 2								
Interception (%)	69 (32)	77 (36)	130 (60)	30 (14)	46 (21)	75 (35)	50 (23)	216 (100)
No-go (%)	31 (14)	41 (19)	72 (33)	29 (13)	29 (13)	31 (14)	31 (14)	216 (100)

D = direction; A = acceleration; T = TMT. The "×" sign indicates interaction terms.

ods), in which the activity of a given motor cortical neuron is related to the hand position, velocity, and first-order estimate of time-to-interception (τ) based on the hand movement. Since the direction of interception movement was always upward, only the neurons with significant directional tuning (Lurito, Georgakopoulos, & Georgopoulos, 1991) and preferred directions within 45° of the direction of interception were included in this analysis. A total of 137 neurons (16%) met both of these criteria. In almost all

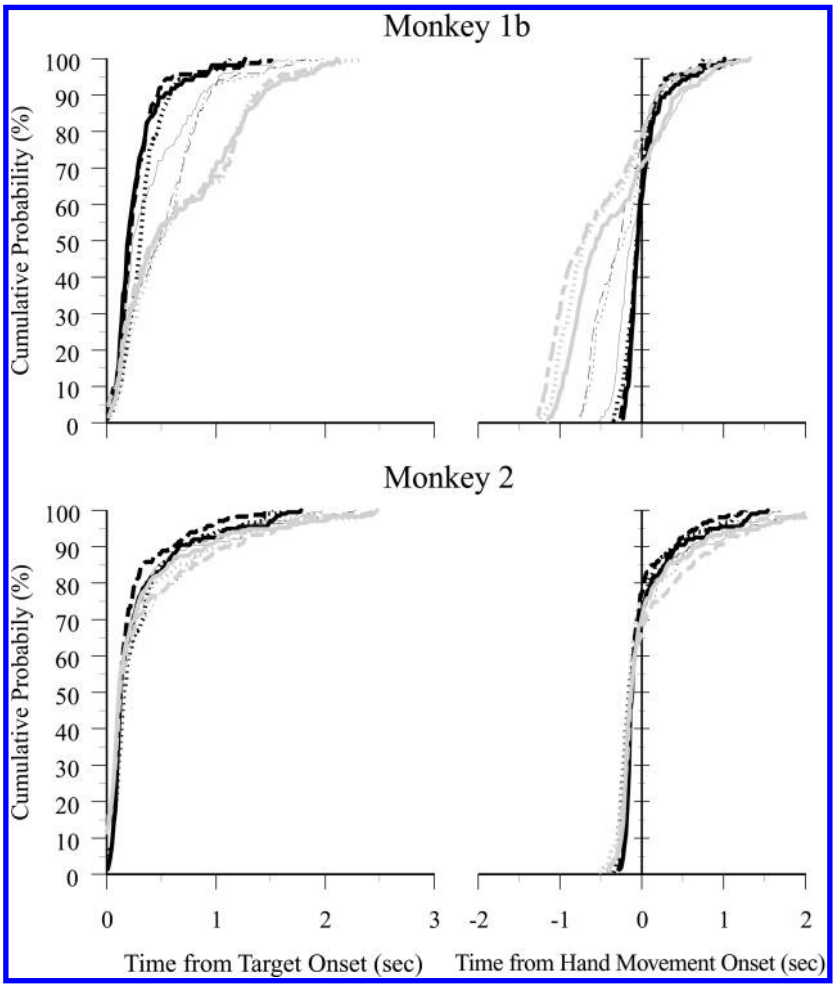

Figure 7. Cumulative probability functions for onset times of neuronal activity in the interception task relative to target onset (left) and movement onset (right). TMT is indicated by the line types: thick black lines = 0.5 sec; thin lines = 1.0 sec; thick gray lines = 1.5 sec. Target acceleration type is indicated by different line types: dotted line = constant acceleration; dashed line = constant deceleration; continuous line = constant velocity.

Table 3. Mean Onset Times for Neural Activity in the No-Go Task

Acceleration	*Accelerating*			*Decelerating*			*Constant Velocity*		
TMT	*0.5*	*1.0*	*1.5*	*0.5*	*1.0*	*1.5*	*0.5*	*1.0*	*1.5*
Monkey 1b	0.346	0.504	0.792	0.317	0.447	0.504	0.302	0.471	0.662
Monkey 2	0.336	0.502	0.600	0.246	0.472	0.526	0.286	0.469	0.638

Only the onset times that are shorter than the TMT + 0.5 sec were included in calculating the mean.

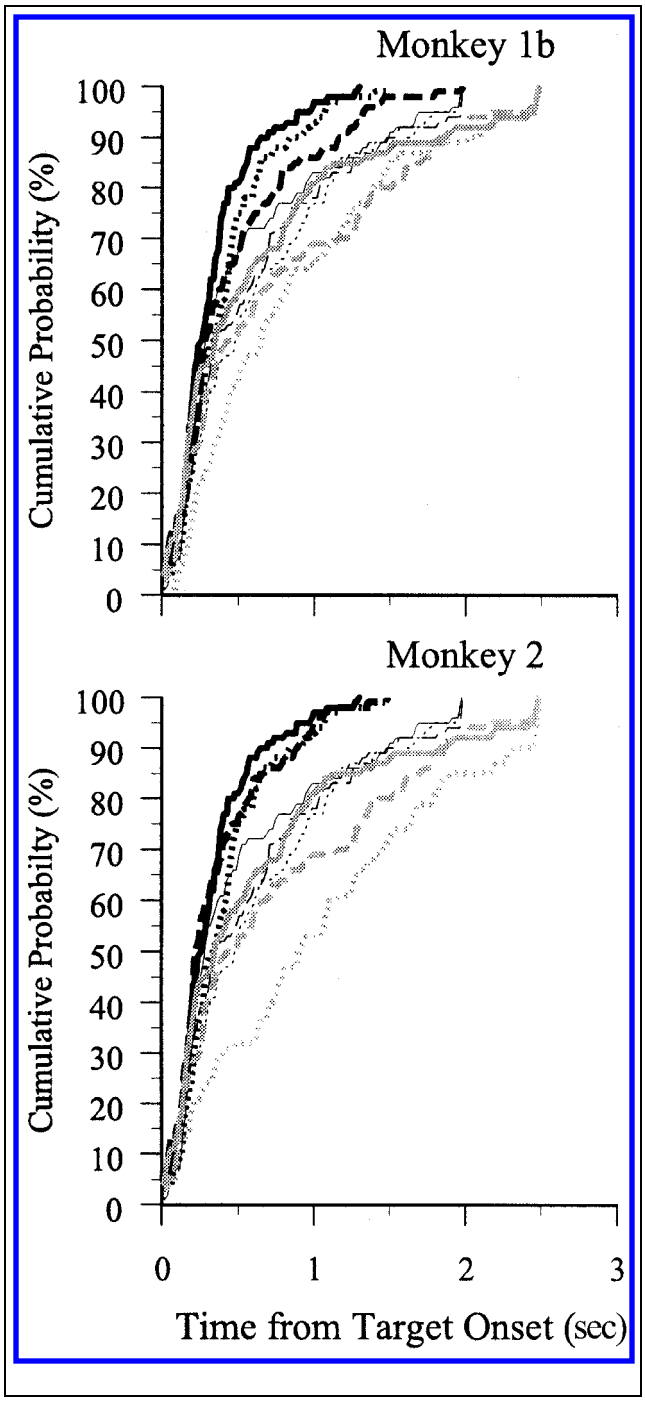

Figure 8. Cumulative probability function for onset times of neuronal activity in the no-go task relative to target onset. The same convention as in Figure 7.

of these neurons (99%), the regression model with three independent parameters (i.e., hand position, velocity, and τ) provided a statistically significant fit to the data (F test, $p < .05$).

To determine whether activity of motor cortical neurons is related to the first-order estimate of time-to-interception (τ), the percentage of neurons in which each of the regression variables was significant was calculated. On average, 91%, 84%, and 62% of the neurons displayed significant relationship with hand position, velocity, and τ, respectively. Thus, substantial fraction of neurons in the motor cortex modulated their activity in accordance with τ, although this effect was not seen as frequently as those of hand position or velocity. Similar results were obtained when the same three variables were rank-ordered according to their absolute values of standardized regression coefficients in a given neuron. The percentages of neurons in which the hand position, velocity, and τ were most significant were 20%, 61%, and 19%, respectively. On the other hand, the number of neurons in which only one of these variables was significant was relatively small. About half of the neurons displayed significant relationship with all three independent variables (Figure 9).

The distributions of signs of regression coefficients were not even. The percentages of neurons with positive regression coefficients for position, velocity, and τ were 32%, 69%, and 34%, respectively. All of these

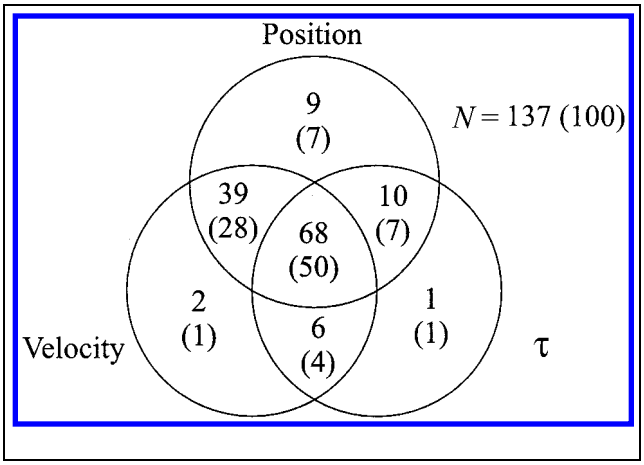

Figure 9. Number of neurons showing significant effects of hand position, velocity, and τ as well as their various combinations. Numbers in parentheses indicate the percentages.

values were significantly different from 50% (binomial test, $p < .001$), consistent with the fact that these neurons were prescreened for their upward directional tuning. For position, there were more neurons with negative coefficients, and this is expected because hand displacement was expressed in the model as the distance between the hand position and the interception point. The fact that there were more neurons with negative coefficients for τ indicates that its contribution in the motor cortical activity is to increase the activity near the time of interception.

DISCUSSION

Individual Difference in the Behavioral Strategies for Target Interception

This experiment was designed to probe the dynamic interaction between a moving visual stimulus and the movement aimed to intercept it. The experimentally controlled stimulus parameters included the direction, duration, and pattern of stimulus motion. As has been found in human studies (Lee et al., 1997; Port et al., 1997), the latter two parameters, and especially the duration of stimulus motion, were the major determinants of the motor behavior in this task. Specifically, short TMT (e.g., 0.5 sec) enforce fast reaction and short movement times, whereas longer TMT (e.g., 2 sec) allow the adoption of different strategies by different subjects. In the previous studies on human subjects, it was found that for long TMT, some subjects initiated their movements immediately after target onset whereas others delayed the initiation of their movements progressively as TMT increased (Port et al., 1997). In the current study, similar difference in behavioral strategy was found in monkeys. Monkey 1 altered its reaction times substantially according to TMT, whether oculomotor fixation was required (Monkey 1b) or not (Monkey 1a), suggesting that oculomotor control was not an important factor in determining behavioral strategies in the present interception task. In addition, these different behavioral strategies remained stable throughout the training and recording sessions that took place over a period of several months. The monkeys gained substantially more practice in the interception tasks than did the human subjects in our previous studies. Nevertheless, these results are consistent with our previous finding that in our interception task, behavioral strategies were relatively unaffected by practice (Port et al., 1997).

Motor Cortical Activity During the No-Go Task

Most neurons (93%) examined in this study were active during both the interception and the no-go task. These results indicate that the hand movement per se is not necessary for activity changes in the motor cortex. This has been demonstrated in many studies using instructed delay tasks and stationary visual targets (see Georgopoulos, 1994, for a review). The present study confirms the existence of substantial activity during a no-go task in the primary motor cortex (Miller, Riehle, & Requin, 1992). The magnitude of changes in population activity during the no-go task differed for the two animals examined (Figure 6). This might be due to addition of oculomotor control or blocking of no-go task trials in Monkey 1b. The question still arises as to whether this activity during the no-go task is preparatory to the movement that might be still planned but not executed (Snyder, Batista, & Andersen, 1997). In the present study, changes in activity during the no-go task were systematically related to various aspects of target motion such as TMT and target acceleration. Therefore, it is unlikely that this activity represents nonspecific preparatory signal. Nevertheless, it remains possible that it reflects a preparatory signal, which is in turn related to the target parameters. Further experiments would be required to identify the functional role of the no-go activity in the primary motor cortex.

Neuronal activity during performance of the no-go task has been examined using stationary visual targets in the premotor cortex and parietal area 5 during preparation and generation of movements towards stationary visual stimuli (Kalaska & Crammond, 1995). These two cortical areas displayed markedly different patterns of activity between go and no-go tasks. In the premotor cortex, an initial increase in activity was found immediately after presentation of the visual cue in both tasks, but this activity dissipated quickly in the no-go task. In contrast, in the parietal area 5, activity was almost identical between the two tasks throughout the cue and delay period and diverged only at the end of the delay period. Neither of these patterns could completely describe the pattern of neural activity in the primary motor cortex during presentation of moving targets in the interception and no-go tasks. Activity during the no-go task in the present study was substantially smaller than that found during the interception task throughout the period of target motion, including the initial response. In order to determine to what degree these differences are related to characteristics of the target (moving vs. stationary) as opposed to properties of different cortical areas, it would be necessary to examine the pattern of neural activity in the premotor and parietal cortex during interception and no-go tasks involving moving targets. Nevertheless, one can speculate on the source of motor cortical activity during the no-go task based upon its temporal characteristics. Compared to activity in the premotor cortex during a no-go task with stationary visual stimuli, motor cortical activity during the no-go task with moving targets was more sustained, although its magnitude was much smaller than that found in the interception task. In this regard, motor

cortical activity during the no-go task in the current study is more similar to that found in area 5 (Kalaska & Crammond, 1995). These findings support the hypothesis advanced previously (Kalaska, Caminiti, & Georgopoulos, 1983) that motor cortex and area 5 might process visuomotor information in a similar fashion. These results are also consistent with the fact that the location of neural recordings in the present experiments were from territories interconnected with area 5, namely the crown and part of the exposed part of the precentral gyrus (Caminiti, Zeger, Johnson, Urbano, & Georgopoulos, 1985).

Serial Versus Parallel Processing of Information About Target and Movement

If one assumes that the sensory analysis of information about a moving target and the preparation of movement occur serially and independently, as implied in some behavioral models, such as the threshold distance and threshold τ models, one may expect distinct neural correlates of these two separate processes. Under such a simple hypothesis, neural activity during the no-go task would represent the neural correlate of sensory processing. In that case, onset times of neural activity between the interception and no-go task would be strongly correlated. In contrast, we found only a weak correlation in the onset times between these two tasks. In addition, motor cortical activity during the no-go task often persisted throughout the TMT. These results are not consistent with sequential recruitment of sensory and motor modules (Sternberg, 1969), but suggest, instead, that information about a moving target and the planning of an upcoming interception movement are processed in parallel and overlapping fashion in the motor cortex (Miller et al., 1992). The exact manner in which analysis of sensory information and preparation of behavioral response are manifested in activity of individual neurons may be determined by various factors, including requirements of the behavioral paradigm and prior experience of the subject. In the interception task used in the present study, it is likely that those processes related to preparation and production of movement occur concurrently with those concerned with the analysis of sensory information about the moving target. This is because in the present study the direction and amplitude of the movement necessary to intercept the target remained constant and therefore did not depend on information derived from the target. Thus, more distinct sensory and movement-related activity may be revealed by utilizing an interception paradigm in which more extensive analysis of target characteristics is required for the subject to specify the temporal and spatial characteristics of the movement needed for accurate target interception.

Representation of Movement Parameters in the Motor Cortex

The activity of motor cortical neurons is modulated in accordance with hand position and velocity (Ashe & Georgopoulos, 1994; Schwartz, 1994; Flament & Hore, 1988; Hamada, 1981; Hamada & Kubota, 1979; Humphrey et al., 1970). In the present study, we extended this finding into a situation in which the movement is constrained to intercept a moving target at a predetermined location. In this task, the approaches of the hand and the target toward the interception zone must be coordinated temporally as well as spatially. The results of our regression analysis raises an interesting possibility that achieving such a goal may be facilitated at least in part by the modulation of motor cortical activity according to the time-to-target interception. Approximately two-thirds of the neurons in the motor cortex showed a significant relationship between their activity and the first-order estimate of time-to-interception. However, it must be also noted that the nature of evidence provided in the present study is entirely correlational. Currently, whether reflection of time-to-interception in the motor cortical activity has any functional significance remains unknown.

METHOD

Animals

Two male rhesus monkeys (*Macaca mulatta*, 8–11 kg body weight; referred to as Monkeys 1 and 2) were used. Monkeys 1 and 2 used their right and left hands in performing the tasks, respectively, and recordings were made from the hemisphere contralateral to the performing arm. The motor cortex of Monkey 1 was recorded from in two separate sessions. In the first session (1a), the monkey was allowed to make free eye movements whereas in the second session (1b), it was required to fixate a stationary target during task performance. For Monkey 2, there were no restrictions on eye movements. Care and treatment of the animals during all stages of the experiments conformed to the principles outlined in Principles of Laboratory Animal Care (NIH Publication No. 86-23, revised 1995).

Apparatus

All visual stimuli were displayed on a 14-in. color computer monitor (Gateway 1020NI) located 57 cm away from the monkey at approximately eye level. The monitor was adjusted for a screen resolution of 640 horizontal and 480 vertical pixels, with a refresh rate of 60 Hz. The animals were seated in a primate chair and controlled the feedback cursor displayed on the monitor by moving a two-dimensional articulated manipulandum on a horizontal planar working surface. The apparatus has been described previously (Georgopoulos, Kalaska, &

Massey, 1981). The monkeys grasped the distal end of the manipulandum with their pronated hand while the other hand was comfortably restrained in a large acrylic tube. The position of the manipulandum in x–y coordinates was digitally sampled at a rate of 100 Hz, and with a spatial resolution of 0.125 mm. The gain was set to one, so that movement of the feedback cursor had a one-to-one correspondence with that of the manipulandum. A personal computer was used for experimental control, visual presentation, and data collection.

Behavioral Tasks

Three tasks were used, namely (a) moving the hand to intercept a moving target (interception task), (b) remaining immobile during presentation of the same moving visual stimulus (no-go task), and (c) moving to stationary targets in eight radial directions (center-out task). This report focuses on the comparison of neural activity in the primary motor cortex between the first two tasks. Part of the results obtained from the center-out task is presented in the companion article (Lee et al., 2001).

In the interception task (Figure 1, left), the stimulus (a) traveled in a straight line and at 45° from either lower corner of the computer monitor towards the interception point at 12 o'clock direction (two target motion directions), (b) moved with constant velocity, constant acceleration, or constant deceleration (three target acceleration types), and (c) moved for a duration of 0.5, 1.0, and 1.5 sec (three TMTs). Eighteen classes of trials were generated by the combination of these three target parameters, and each combination was presented two to three times in a pseudorandom sequence. Accelerating targets had a starting velocity of 3.0 cm/sec and underwent an appropriate constant acceleration to achieve the desired motion time. Decelerating targets had velocity profiles that were mirror images of those of the accelerating targets and underwent constant deceleration to end with a velocity of 3.0 cm/sec. Constant velocity targets traveled at the appropriate constant velocity to achieve the required motion time.

A trial in the interception task began when the monkey moved the feedback cursor (0.3-cm radius circle) into a start zone (1-cm radius circle for Monkey 1 and 0.5-cm radius circle for Monkey 2) centered at the bottom of the screen along the vertical meridian (Figure 1, left). After the monkey had maintained this position for a random period of 1–3 sec (the start–hold period), a target (0.6-cm radius circle) appeared in the lower right or left corner of the screen. The target then traveled along a 45° path until it reached the vertical meridian of the screen, where it stopped at a location 12.5 cm directly above the center of the start zone. The monkey was required to move the feedback cursor to intercept the target just as it reached its final position at the center of the interception zone. This zone was an invisible positional window, namely a 1.2-cm radius circle for Monkey 1 and a 1.0-cm radius circle for Monkey 2, centered on the final target location. The following conditions were required for a trial to be considered successful. First, the monkey had to maintain the cursor within the start zone until 130 msec after target onset. This condition was imposed to prevent anticipatory movements to the target. Second, the monkey had to move the manipulandum so that the feedback cursor would enter the interception zone within 130 msec of the target's arrival at the interception point. And third, after the cursor entered the interception zone, the monkey had to maintain the cursor within an invisible, 2.0 cm radius, circular positional window (target hold zone) for 0.5 sec. Trials were aborted when any of the above listed conditions was violated. Monkeys were notified of unsuccessful trials with a tone, and rewarded for successful trials with a drop of juice. There were no other constraints on the animal's movements or their initiation.

The no-go task was used in recordings from Monkeys 1b and 2. In this task, the monkey was trained to withhold the movement. No-go trials were indicated to the monkey at the beginning of a trial by a change in color of the hold zone. Following the start–hold period, the target appeared and began moving towards the interception zone just as in the interception trials but the trial was aborted if the monkey moved the manipulandum more than 1 cm at any time up to the delivery of the reward. After the target reached the interception zone, it remained there for 0.5 sec until the monkey was rewarded with a drop of juice.

Finally, the center-out task (Figure 1, right) was similar to that used previously (Georgopoulos, Kalaska, Caminiti, & Massey, 1982). The start zone was located at the center of the screen. After the start–hold period, a stationary target appeared in one of eight equally spaced positions, every 45°, on an imaginary circle of 8 cm radius. For these trials, the monkeys had to move the cursor to the target within 3 sec and hold it there for 0.5 sec to get a reward.

Experimental Design

Eighteen combinations of two directions, three acceleration types, and three TMT were presented in a randomized block design. For Monkey 1a, two stimulus directions were nested within each combination of acceleration and TMT, and were presented in subblocks of two to three trials; in Monkeys 1b and 2, stimulus directions were completely randomized within a combination block. The no-go and interception trials were presented in blocks for Monkey 1b, whereas they were completely randomized for Monkey 2. Eight trials of the center-out task (one for each radial direction) were randomly mixed within each combination block, which was repeated five, three, and four times for

Monkeys 1a, 1b, and 2, respectively. Therefore, a given neuron was tested in at least 45, 54, and 72 trials for the interception task for Monkeys 1a, 1b, and 2, respectively, and the same number of trials for the no-go task. Unsuccessful trials were rerandomized and repeated until correct performance was achieved. This was done to obtain an equal number of successful trials for all target conditions.

Data Collection

Neural Recording

After an animal was trained to perform with greater than 85% accuracy in the task, recordings of cortical neurons during task performance were initiated using a seven-electrode recording system (UWE THOMAS, Marburg, Germany; see Lee, Port, Kruse, & Georgopoulos, 1998; Mountcastle, Reitboeck, Poggio, & Steinmetz, 1991). The electrophysiological techniques used to record the extracellular electrical signals of single cell activity, the surgical procedures, and the animal care have been described previously (Lurito et al., 1991; Georgopoulos et al., 1982). All surgical procedures were performed under general anesthesia and aseptic conditions. In the present experiments we used a lightweight metal halo (Nakasawa Works, Tokyo, Japan) to stabilize the head during recording sessions. Neural impulses were discriminated online using dual-time–amplitude window discriminators (BAK Electronics, MD) and computer-controlled spike template matching (Alpha Omega Engineering, Nazareth, Israel).

Eye Position Recordings

For Monkey 1, eye position was monitored by the sclera search coil method (Fuchs & Robinson, 1966; CNC Engineering, Seattle, WA); the coil was surgically implanted using the method of Judge, Richmond, and Chu (1980). For Monkey 2, eye position was monitored by an infrared oculometer (DR. BOUIS, Karlsruhe, Germany). Horizontal and vertical eye positions were sampled at 200 Hz. Once again, for recordings in Monkeys 1a and 2, there were no restrictions on eye movements, and eye position data were collected throughout the trial. However, in recording Monkey 1b, the animal was required to fixate within 2° of the visual angle from the center of the start zone throughout the trial. The trial was aborted if visual fixation was broken at any time during the trial.

Electromyographic Recordings

The EMG activity was recorded during performance of the task using intramuscular, Teflon-coated, multistranded stainless steel wires. The sampled muscles included anterior deltoid, posterior deltoid, upper trapezius, pectoralis, biceps, triceps, supraspinatus, and infraspinatus. The EMG recordings were done separately from the neural recordings sessions. The EMG signals were recorded differentially, amplified through a Grass amplifier system with an amplification of 10,000–20,000, band-pass filtered at 30–300 Hz, sampled at a rate of 1 kHz, and rectified.

Histology

After the experiments were completed, the area of recording was demarcated on the cortical surface using metal pins inserted at known recording locations using a microdrive placement system. The animal was then euthanized by a lethal overdose of sodium pentobarbital, perfused transcardially with buffered formalin, fixed, and the brain removed for histological processing.

Data Analysis

General

Standard statistical analyses (Snedecor & Cochran, 1989; Winer, 1971) were used, including paired t tests, repeated measures analysis of variance (ANOVA), and covariance (ANCOVA). A level of $p < .05$ was regarded as statistically significant for rejecting the null hypothesis that the variation was due to chance. Ad hoc computer programs and commercially available statistical packages (SPSS, version 7, SPSS, Chicago, IL, 1996; BMDP/DYNAMIC, BMDP Statistical Software, Los Angeles, CA, 1993) were used for statistical analyses. Specifically, the program 5V of BMDP was used for the repeated measures ANOVA and ANCOVA analyses.

Analysis of Behavioral Data

The hand position was smoothed and differentiated using the finite impulse response method (passband 0–0.5 Hz; stopband 13–50 Hz). For any given movement, the response time (RT) was defined as the first time at which hand velocity reached 10% of its peak velocity. The movement time (MT) was defined as the period between the response time and the last time at which the hand decreased in velocity below 10% of its peak velocity. Finally, the total experimental time (TET) was: TET = RT + MT.

We analyzed the response times in the interception task, using the threshold distance and threshold τ models. We have previously applied these models to the response time data obtained from human subjects (Port et al., 1997). In the threshold distance model, it is assumed that the movement is initiated after a constant processing time from the moment when the position of the target has traveled the threshold distance from its

starting position (Collewijn, 1972). In the threshold τ model, it is assumed that the movement is initiated after a constant processing time from the moment when the first-order estimate of time to arrival of the target at its destination reaches a certain threshold. This estimate of time-to-target arrival is referred to as "τ" (τ), which can be calculated as the distance between the target's current position and its destination divided by its current velocity (Lee, 1976). The equations used to derive the response times predicted by either of these two models as well as the nonlinear curve fitting procedure have been described in detail previously (Port et al., 1997).

Categorization of Neurons

For each neuron, the total number of spikes in all tasks was determined, and neurons with less than 50 spikes were excluded from the analysis. Of particular interest was to determine if cell activity varied significantly with parameters of moving targets in the interception and no-go tasks. To this end, all main effects of target parameters and their interactions were assessed using ANOVA and ANCOVA. In ANOVA, we tested whether change in cell activity during TET varied significantly across different target conditions, whereas in ANCOVA, we tested whether cell activity during TET varied significantly across target conditions, using the activity during the start–hold period as a trial-by-trial covariate (Snedecor & Cochran, 1989). For the no-go task, activity during TMT was analyzed instead of TET since there was no movement. A cell was deemed to be unrelated to a given task if none of the main effects and none of the interactions were statistically significant; if any of these factors was significant, then the cell was deemed to be related to the particular task.

Spike Density Function

The spike train was converted to a spike density function for some analyses (MacPherson & Aldridge, 1979). This was calculated using the fixed kernel method of Richmond, Optican, Podell, and Spitzer (1987) using a Gaussian pulse width of 30 msec. We also used average spike density functions synchronized with target or movement onset to determine the relative timing of neural activity related to either of these events. This procedure was performed separately for every combination of TMT and target acceleration type. The onset of activity was defined as the earliest time when the average spike density function exceeded the baseline activity (taken during the 500 msec period before the target onset) by more than three times the standard deviation of the baseline spike density function (MacPherson & Aldridge, 1979). For onset time relative to target onset, the spike density function was checked against this criterion every 10 msec starting from target onset, whereas for movement-related activity, this procedure was initiated 500 msec before the movement onset.

Spike density functions of individual neurons were averaged to generate population spike density functions (Figure 4). Statistical significance of the modulation in the population spike density function during the no-go task was assessed by a permutation test, in which the temporal relationship between the target onset and the spike density functions was randomized for individual neurons. This procedure was repeated 10,000 times and the p value was calculated as the frequency of shuffles that resulted to a peak in the simulated data that was higher than the peak of the actual data.

Multiple Linear Regression

The nature of interception task requires a tight temporal coupling between the hand movement and target motion. It is, therefore, reasonable to ask whether information about the time-to-target acquisition is systematically represented in the pattern of motor cortical activity. To examine this possibility, we applied the following regression model:

$$\mathrm{sdf}(t+\Delta t) = a0 + a1\mathrm{d}(t) + a2\mathrm{d}'(t) + a3\tau(t) + \varepsilon(t), \quad t \in T,$$

where $\mathrm{sdf}(t)$ is the spike density function at time t, $\mathrm{d}(t)$ and $\mathrm{d}'(t)$ are the vertical distance between the hand position at time t and the lower boundary of the interception zone and its time derivative, $\tau(t) = \mathrm{d}(t)/\mathrm{d}'(t)$, $\varepsilon(t)$ is the error term, Δt is a time-shift between the spike density function and the kinematic variables, and $a0$–$a3$ are the regression coefficients. T refers to the period between the time when the hand reaches 10% of its peak velocity in a given trial and the time when the hand arrives at the interception zone. It has been shown in a previous study that in the motor cortex, the best fit between the motor cortical activity and the kinematic variables is achieved by a time-shift of about −100 msec (Ashe & Georgopoulos, 1994). Therefore, in this study, the time-shift was fixed at −100 msec. Hand acceleration was not included in this model, because it has relatively little effect on the motor cortical activity (Ashe & Georgopoulos, 1994).

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REFERENCES

Ashe, J., & Georgopoulos, A. P. (1994). Movement parameters and neural activity in motor cortex and area 5. *Cerebral Cortex, 4,* 590–600.

Caminiti, R., Zeger, S., Johnson, P. B., Urbano, A., & Georgopoulos, A. P. (1985). Corticocortical efferent systems in the monkey: A quantitative spatial analysis of the tangential distribution of cells of origin. *Journal of Comparative Neurology, 241,* 405–419.

Collewijn, H. (1972). Latency and gain of the rabbit's optokinetic reactions to small movements. *Brain Research, 36,* 59–70.

Flament, D., & Hore, J. (1988). Relations of motor cortex neural discharge to kinematics of passive and active elbow movements in the monkey. *Journal of Neurophysiology, 60,* 1268–1284.

Fuchs, A. F., & Robinson, D. A. (1966). A method for measuring horizontal and vertical eye movements chronically in the monkey. *Journal of Applied Physiology, 21,* 1068–1070.

Georgopoulos, A. P. (1994). New concepts in generation of movement. *Neuron, 13,* 257–268.

Georgopoulos, A. P., Kalaska, J. F., Caminiti, R., & Massey, J. T. (1982). On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. *Journal of Neuroscience, 2,* 1527–1537.

Georgopoulos, A. P., Kalaska, J. F., & Massey, J. T. (1981). Spatial trajectories and reaction times of aimed movements: Effects of practice, uncertainty and change in target location. *Journal of Neurophysiology, 46,* 725–743.

Hamada, I. (1981). Correlation of monkey pyramidal tract neuron activity to movement velocity in rapid wrist flexion movement. *Brain Research, 230,* 384–389.

Hamada, I., & Kubota, K. (1979). Monkey pyramidal tract neurons and changes of movement parameters in visual tracking. *Brain Research Bulletin, 4,* 249–257.

Humphrey, D. R., Schmidt E. M., & Thompson, W. D. (1970). Predicting measures of motor performance from multiple cortical spike trains. *Science, 170,* 758–762.

Judge, S. J., Richmond, B. J., & Chu, F. C. (1980). Implantation of magnetic search coils for measurement of eye position: An improved method. *Vision Research, 20,* 535–538.

Kalaska, J. F., Caminiti, R., & Georgopoulos, A. P. (1983). Cortical mechanisms related to the direction of two-dimensional arm movements: Relations in parietal area 5 and comparison with motor cortex. *Experimental Brain Research, 51,* 247–260.

Kalaska, J. F., & Crammond, D. J. (1995). Deciding not to go: Neuronal correlates of response selection in a go/nogo task in primate premotor and parietal cortex. *Cerebral Cortex, 5,* 410–428.

Lee, D. N. (1976). A theory of visual control of braking based on the information about time-to-contact. *Perception, 5,* 437–459.

Lee, D., Port, N. L., & Georgopoulos, A. P. (1997). Manual interception of moving targets: II. Online control of overlapping submovements. *Experimental Brain Research, 116,* 421–433.

Lee, D., Port, N. L., Kruse, W., & Georgopoulos, A. P. (1998). Neuronal population coding: Multielectrode recordings in primate cerebral cortex. In H. Eichenbaum & J. Davis (Eds.), *Neuronal ensembles: Strategies for recording and decoding* (pp. 117–136). New York: Wiley.

Lee, D., Port, N. L., Kruse, W., & Georgopoulos, A. P. (2001). Neuronal clusters in the primate motor cortex during interception of moving targets. *Journal of Cognitive Neuroscience 13,* 319–331.

Lurito, J. T., Georgakopoulos, T., & Georgopoulos, A. P. (1991). Cognitive spatial–motor processes: 7. The making of movements at an angle from a stimulus direction: Studies of motor cortical activity at the single cell and population levels. *Experimental Brain Research, 87,* 562–580.

MacPherson, J. M., & Aldridge, J. W. (1979). A quantitative method of computer analysis of spike train data collected from behaving animals. *Brain Research, 175,* 183–187.

Miller, J., Riehle, A., & Requin, J. (1992). Effects of preliminary perceptual output on neuronal activity of the primary motor cortex. *Journal of Experimental Psychology: Human Perception and Performance, 18,* 1121–1138.

Mountcastle, V. B., Reitboeck, H. J., Poggio, G. F., & Steinmetz, M. A. (1991). Adaptation of the Reitboeck method of multiple microelectrode recording to the neocortex of the waking monkey. *Journal of Neuroscience Methods, 36,* 77–84.

Port, N. L., Lee, D., Dassonville, P., & Georgopoulos, A. P. (1997). Manual interception of moving targets: I. Performance and movement initiation. *Experimental Brain Research, 116,* 406–420.

Port, N. L., Lee, D., Kruse, W., & Georgopoulos, A. P. (1996). Motor cortical activity during target motion in the presence and absence of manual target interception. *Society for Neuroscience Abstract, 22,* 12.

Richmond, B. J., Optican, L. M., Podell, M., & Spitzer, H. (1987). Temporal encoding of two-dimensional patterns by single units in primate inferior temporal cortex: I. Response characteristics. *Journal of Neurophysiology, 57,* 132–146.

Schwartz, A. B. (1994). Direct cortical representation of drawing. *Science, 265,* 540–542.

Snedecor, G. W., & Cochran, W. G. (1989). *Statistical methods.* Ames, Iowa: Iowa State University Press.

Snyder, L. H., Batista, A. P., & Andersen, R. A. (1997). Coding of intention in the posterior parietal cortex. *Nature, 386,* 167–170.

Sternberg, S. (1969). The discovery of processing stages: Extensions of Donder's method. *Acta Psychologica, 30,* 276–315.

van Donkelaar, P., Lee, R. G., & Gellman, R. S. (1992). Control strategies in directing the hand to moving targets. *Experimental Brain Research, 91,* 151–161.

Winer, B. J. (1971). *Statistical principles in experimental design* (2nd ed.). New York: McGraw–Hill.

Wise, S. P., Boussaoud, D., Johnson, P. B., & Caminiti, R. (1997). Premotor and parietal cortex: Corticocortical connectivity and combinatorial computations. *Annual Review of Neuroscience, 20,* 25–42.

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3. C.-S. Ray Li. Response Inhibition 303-317. [Crossref]
4. Alexandra Battaglia-Mayer, Tania Buiatti, Roberto Caminiti, Stefano Ferraina, Francesco Lacquaniti, Tim Shallice. 2014. Correction and suppression of reaching movements in the cerebral cortex: Physiological and neuropsychological aspects. *Neuroscience & Biobehavioral Reviews* **42**, 232-251. [Crossref]
5. G. Mirabella, P. Pani, S. Ferraina. 2011. Neural correlates of cognitive control of reaching movements in the dorsal premotor cortex of rhesus monkeys. *Journal of Neurophysiology* **106**:3, 1454-1466. [Crossref]
6. Osamu Hiwaki, Naoyuki Ishimaru, Hiroshi Fukuda. Disturbance on inhibitory control of reaching finger movement caused by transcranial magnetic stimulation 638-641. [Crossref]
7. Joost C. Dessing, Leonie Oostwoud Wijdenes, C. (Lieke) E. Peper, Peter J. Beek. 2009. Adaptations of lateral hand movements to early and late visual occlusion in catching. *Experimental Brain Research* **192**:4, 669-682. [Crossref]
8. Giovanni Mirabella, Pierpaolo Pani, Stefano Ferraina. 2009. The presence of visual gap affects the duration of stopping process. *Experimental Brain Research* **192**:2, 199-209. [Crossref]
9. Hugo Merchant, Oswaldo Pérez. Neurophysiology of Interceptive Behavior in the Primate: Encoding and Decoding Target Parameters in the Parietofrontal System 191-206. [Crossref]
10. Patrice Senot, Sylvain Baillet, Bernard Renault, Alain Berthoz. 2008. Cortical Dynamics of Anticipatory Mechanisms in Interception: A Neuromagnetic Study. *Journal of Cognitive Neuroscience* **20**:10, 1827-1838. [Abstract] [PDF] [PDF Plus]
11. H. Zhang, N. Ye, J. He, A. Roontiva, J. Aguayo. Two-way ANOVA to identify impacts of multiple interactive behavioral factors on the neuronal population dependency during the reaching motion 1335-1338. [Crossref]
12. Romi Nijhawan. 2008. Visual prediction: Psychophysics and neurophysiology of compensation for time delays. *Behavioral and Brain Sciences* **31**:02. . [Crossref]
13. James R. Carey, Kristine R. Greer, Tiffany K. Grunewald, Jennifer L. Steele, Jeff W. Wiemiller, Ela Bhatt, Ashima Nagpal, Ovidiu Lungu, Edward J. Auerbach. 2006. Primary Motor Area Activation during Precision-Demanding versus Simple Finger Movement. *Neurorehabilitation and Neural Repair* **20**:3, 361-370. [Crossref]
14. Giovanni Mirabella, Pierpaolo Pani, Martin Paré, Stefano Ferraina. 2006. Inhibitory control of reaching movements in humans. *Experimental Brain Research* **174**:2, 240-255. [Crossref]
15. H. Merchant. 2005. Neurophysiology of Perceptual and Motor Aspects of Interception. *Journal of Neurophysiology* **95**:1, 1-13. [Crossref]
16. Myrka Zago, Francesco Lacquaniti. 2005. Internal Model of Gravity for Hand Interception: Parametric Adaptation to Zero-Gravity Visual Targets on Earth. *Journal of Neurophysiology* **94**:2, 1346-1357. [Crossref]
17. Joost C. Dessing, C. (Lieke) E. Peper, Daniel Bullock, Peter J. Beek. 2005. How Position, Velocity, and Temporal Information Combine in the Prospective Control of Catching: Data and Model. *Journal of Cognitive Neuroscience* **17**:4, 668-686. [Abstract] [PDF] [PDF Plus]
18. Joost C. Dessing, Simone R. Caljouw, C. (Lieke) E. Peper, Peter J. Beek. 2004. A dynamical neural network for hitting an approaching object. *Biological Cybernetics* **91**:6, 377-387. [Crossref]
19. Iver H. Iversen, Tetsuro Matsuzawa. 2003. Development of interception of moving targets by chimpanzees (Pan troglodytes) in an automated task. *Animal Cognition* **6**:3, 169-183. [Crossref]
20. Emilio Salinas. 2003. Background Synaptic Activity as a Switch Between Dynamical States in a Network. *Neural Computation* **15**:7, 1439-1475. [Abstract] [PDF] [PDF Plus]
21. Michael T.V Johnson, Carolyn R Mason, Timothy J Ebner. 2001. Central processes for the multiparametric control of arm movements in primates. *Current Opinion in Neurobiology* **11**:6, 684-688. [Crossref]
22. H. Merchant, A. Battaglia-Mayer, A. P. Georgopoulos. 2001. Effects of Optic Flow in Motor Cortex and Area 7a. *Journal of Neurophysiology* **86**:4, 1937-1954. [Crossref]
23. Daeyeol Lee, Nicholas L. Port, Wolfgang Kruse, Apostolos P. Georgopoulos. 2001. Neuronal Clusters in the Primate Motor Cortex during Interceptin of Moving Targets. *Journal of Cognitive Neuroscience* **13**:3, 319-331. [Abstract] [PDF] [PDF Plus]