Deciding Not to GO: Neuronal Correlates of Response Selection in a GO/NOGO Task in Primate Premotor and Parietal Cortex

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Monkeys performed reaching movements in two opposite directions in a symmetrically rewarded GO/NOGO task with an instructed-delay period. Instructional cues were presented at the target locations. The decision not to move was clearly reflected in cell activity in dorsal premotor cortex, but not in parietal cortex area 5. In premotor cortex, the initial response (<250 msec) of most cells to the appearance of the instructional cues in GO and NOGO trials was similar. However, by the end of the delay period, the responses of most cells were statistically different between the two trial types, and the population signals were much less directional in the NOGO trials than in the GO trials. In area 5, in contrast, single-cell and population signals were generally similar and strongly directional in both GO and NOGO trials. This result suggests a role for area 5 in visuomotor analysis for the guidance of limb movements. It further suggests that separate representations of potential motor responses to external inputs and of the intended response to that input can coexist in parietal and premotor cortex, respectively.

The function of area 5 of the primate posterior parietal cortex remains controversial. Previous studies imposed a strict somatosensory versus somatomotor dichotomy (Kalaska, 1988, 1991). For example, a major input to area 5 is from primary somatosensory cortex (SI; Pearson and Powell, 1985) and early single-unit recordings in area 5 revealed cells with more complex passive somatic receptive fields than in SI (Duffy and Burchfiel, 1971; Sakata et al., 1973). As a result, area 5 was viewed as having a higher-order somatosensory role (Sakata et al., 1973). In contrast, subsequent findings of area 5 cells whose activity was unaltered by passive somatic inputs but changed during active movement (Mountcastle et al., 1975; Seal et al., 1982, 1983; Seal and Commenges, 1985), preceded movement onset (Mountcastle et al., 1975; Seal et al., 1982; Kalaska et al., 1983; Chapman et al., 1984; Seal and Commenges, 1985), and covaried with the direction of arm movement (Kalaska et al., 1983, 1990), supported a more motor role. However, this sensory versus motor dichotomy is probably simplistic. Alternatively, the parietal cortex may couple perception to action by contributing to the sensory analyses and sensorimotor transformations required for the control of movement (Stein, 1989; Goodale and Milner, 1992). Since area 5 projects to cortical and subcortical motor structures (Strick and Kim, 1978; Wiesendanger et al., 1979; Petrides and Pandya, 1984), it is well positioned to act as an interface to channel somatic sensory information to the motor system, where it can be used to guide motor behavior (Stein, 1976; Chapman et al., 1984; Nixon et al., 1992).

Recently, the possibility that area 5 may also process visuospatial information required for visually guided movements has received new support. The medial intraparietal region (MIP) of area 5 receives an indirect corticocortical input from visual areas (Colby et al., 1988; Colby and Duhamel, 1991). Deoxyglucose studies of cortical activity during reaching movements indicated that MIP activation was more dependent on visual aspects of the task than the rest of area 5 (Savaki et al., 1993). Furthermore, cells in MIP, the adjacent ventral intraparietal cortex, and dorsolateral area 5 respond to combinations of somatic and visual inputs and may generate a cross-modal representation of the spatial relations between body parts and nearby visual stimuli (MacKay and Crammond, 1987; Colby and Duhamel, 1991; Colby et al., 1993).

Finally, many area 5 cells show directionally tuned changes in activity in instructed-delay tasks during the period between the presentation of visuospatial instructions and signals permitting arm movement (Crammond and Kalaska, 1989; Ferriana and Bianchi, 1994). The role of this delay activity is also uncertain. It could be the neuronal correlate of some aspect of motor planning (Halsband and Passingham, 1982; Seal et al., 1982, 1983; Deiber et al., 1991; Ferriana and Bianchi, 1994), or a corollary discharge about the intended movement that contributes mainly to somatic sensory processes (Kalaska, 1988, 1991; Matthews, 1988).

The motor function of the dorsal premotor cortex, particularly in the selection of appropriate motor responses to external stimuli, is well established (Halsband and Passingham, 1983, 1985; Wise et al., 1983; Weinrich et al., 1984; Passingham, 1989; Mitz et al., 1991; di Pelligrino and Wise, 1993a,b). Comparison of activity in area 5 and premotor cortex in the same task conditions may help clarify area 5 function. To this end we studied the responses of neurons in both areas in an instructed-delay task in which monkeys made four different learned conditional responses to different cues, using an instructed-delay paradigm (Kalaska and Crammond, 1990, 1993; Crammond and Kalaska, 1993, 1994). We report here the behavior of cells in two of the differential response conditions, a symmetrically rewarded GO/NOGO decision.

Materials and Methods

Two male rhesus monkeys (*Macaca mulatta*, 4–5 kg) were trained to make visually guided reaching movements to displace a pendulum-like handle from a central starting position to one of eight equally spaced target locations arrayed in a circle of 8 cm radius (Kalaska et al., 1990). At each target location was a triplet of light-emitting diodes (LEDs; red, green, yellow) that were used to signal intended movement direction in instructed-delay trials of different stimulus–response (SR) compatibility (Crammond and Kalaska, 1994).

Tasks

Eight-Direction Task

All cells were first tested in an eight-direction reaching task (Crammond and Kalaska, unpublished observations). Two types of trials, reaction-time (RT) and direct-delay (DD) trials, were presented with equal probability in a randomized-block sequence (Fig. 1A). Each trial began when the central red LED was illuminated and the monkey moved the handle into the central window (4 mm radius). The monkey held the handle within the central window for a variable center-hold period (2–6 sec), until the red LED was illuminated at one of the target locations. This was the GO signal, at which point the monkey moved the handle to the target (15 mm radius) and held it there for a further 2 sec, to earn a liquid reward. In RT trials, no further stimulus events occurred, so that the monkey had no prior knowledge of the intended movement direction until the presentation of the GO signal (Fig. 1A). In DD trials, a green cue LED was illuminated at one of the target locations 1-3 sec after the beginning of the trial, and remained on for the duration of the delay period until the GO signal occurred (green LED off and red LED on at the same location). In RT trials, a time marker was stored in the trial record at the time at which a cue signal would have been presented if it had been a DD trial. This allowed comparison of cell activity in RT and DD trials at comparable times during the center-hold period, to distinguish activity changes resulting from the appearance of the instructional signal in DD trials from activity changes due to other factors.

Response-Selection Task

Neurons were then tested in a second task designed to identify neuronal events involved in the selection of motor responses to arbitrary visual signals during an instructed-delay period. Instructional signals were presented in two locations, corresponding to the cell's preferred direction in the eight-direction task, and in the diametrically opposite direction. Four different trial types were presented with equal probability (Fig. 1A). The first two trial types were RT and DD trials just described. In the third trial type, redirected-delay (RD) trials (Crammond and Kalaska, 1994), a yellow cue LED at one of the two target locations instructed the monkey to make a movement away from the cue toward the opposite target when the GO signal appeared. In the fourth trial type, NOGO trials, all three colored LEDs were illuminated at one of the two target locations as the cue. This ambiguous signal instructed the monkey to remain at the central location for 2 sec after the appearance of the GO signal (i.e., "pseudo-GO") to receive a reward. The temporal structure of the RD and NOGO trials was identical to the DD trials.

Unlike the eight-direction task, two different GO signals were used in DD, RD, and NOGO trials of the response-selection task, presented randomly with equal probability (Fig. 1A). In half of the trials, only the red LED at the target location was illuminated (spatially matched GO), as in the eight-direction task. In the remaining trials, all eight red target LEDs were illuminated as a nonspatial GO signal. This ensured that the monkey used the information provided by the cues to select the necessary response, and did not simply ignore the instructional cues and wait until the GO LED appeared at the target. Nonspatial GO signals could not be used in RT trials.

Other Task Variants

Some cells were tested in a "memory" (MEM) task to examine to what degree cell activity during the instructed-delay period reflected the motor instructional content of the cue signals or was a "sensory" response to the cue. Movements were made in two opposite directions. Half of the trials were standard DD trials in which the green cue LED remained illuminated for the entire duration of the delay period. In the remaining MEM trials, the green instructional cue was illuminated for a fixed period of 500 msec, after which it was extinguished for the remainder of the variable delay period. Only nonspatial GO signals were used in the MEM task.

To further evaluate the influence of stimulus location on the responses of cells in NOGO trials, selected parietal neurons were tested in a task that involved only NOGO trials. The NOGO cues were presented in two opposite locations as in the response-selection task. However, different combinations of LEDs were used as pseudo-GO signals. In one version, different combinations of one, three, five, seven, or eight red LEDs were illuminated simultaneously as the pseudo-GO signal. In a second version, a red LED at any one of the eight target locations could be illuminated as the pseudo-GO signal, independent of the location of the NOGO cue signals.

Recording

After training, a recording cylinder was implanted over the motor/premotor or parietal cortex contralateral to the trained arm, using standard aseptic surgical methods. Single-cell activity was recorded using glass-insulated Pt-Ir electrodes. Isolated cells were accepted for further study if they were preferentially related to motions about the shoulder joint. Cells that were related to movements of the wrist, hand, or trunk were not studied, even if active in the task. After data collection from one recording cylinder, the monkey was trained to perform the task with the other arm, and a second cylinder was implanted on the contralateral hemisphere, over the cortical region that was not examined in the first hemisphere.

Data Analysis

For quantitative analysis, the trials were divided into a number of behavioral epochs. For this article, the epochs of interest were the first and second 250 msec after the presentation of the cue signal and the last 500 msec of the delay period before the GO signal. The mean discharge rate of the cells during those epochs, including partial spike intervals, was calculated for each trial. These data were used to compare the behavior of the cells in corresponding time intervals in the different trial types, using t tests and correlation analysis.

Muscle Activity

On selected days, EMG activity was recorded from all major shoulder and axial muscles, including the deltoids (three heads), pectoralis major, latissimus dorsi, teres major, infraspinatus, supraspinatus, subscapularis, triceps longus, rostral and caudal trapezius, rhomboids, thoracic and cervical paraspinals, atlantoscapularis anterior and splenius capitis. Pairs of fine Teflon-coated stainless steel wire electrodes were inserted percutaneously into the belly of selected muscles. Identity of the implanted muscles was confirmed by observation of EMG activity during isolated movements outside of the task, and by visual verification of the muscle contractions induced by electrical stimulation via the implanted EMG wires. The rectified and integrated (10 msec bins) EMG signal was then collected during performance of the task.

Results

EMG Activity in GO/NOGO Trials

No change in baseline EMG activity was recorded in response to the cue signals during the delay period of either DD or NOGO trials in all major prime-mover and axial muscles, or after the appearance of the pseudo-GO signal in NOGO trials (Fig. 1B). The only exception in each monkey was the splenius capitis muscle, which showed variable activity changes after the cue and GO signals of both DD trials and NOGO trials. The idiosyncratic behavior of this one muscle was probably explained by the habit of both monkeys of licking and chewing on the reward delivery tube after the presentation of instructional signals in all trials.

Data Base

Several hundred cells were studied in the eight-direction task. Ninety-seven dorsal premotor cells were then selected for study in the response-selection task (42 from monkey B and 55 from monkey C), and 51 cells in parietal area 5 (20 and 31 cells, respectively). We report here the behavior of the cells in DD and NOGO trials of the latter task. The activity of the cells in the other task conditions will be described elsewhere (Crammond and Kalaska, 1994, unpublished observations). For technical reasons, the NOGO responses of four area 5 cells from monkey B could not be analyzed, leaving a data sample of 47 cells. The cortical surface locations of penetration sites are shown in Figure 2. The premotor population was located in the dorsal premotor cortex between the superior precentral sulcus and arcuate sulcus. The parietal sample was recorded in the rostral bank of the intraparietal sulcus, more medially in monkey C than in monkey B (Figs. 2, 3).

Population Responses

The main results of this study are illustrated by the averaged population-response histograms in Figure 4. Premotor cells showed striking differences in their mean responses in DD and NOGO trials, whereas the mean area 5 population activity was virtually identical.

The premotor population showed strong directionally tuned changes in activity in DD trials at the two opposite directions (Fig. 4A,B, outlined histograms; $p < 0.01$, paired t test on the difference in response of each cell for the two movement directions at each time epoch after the cue signal). In NOGO trials (Fig. 4A,B, solid histograms), the short-latency

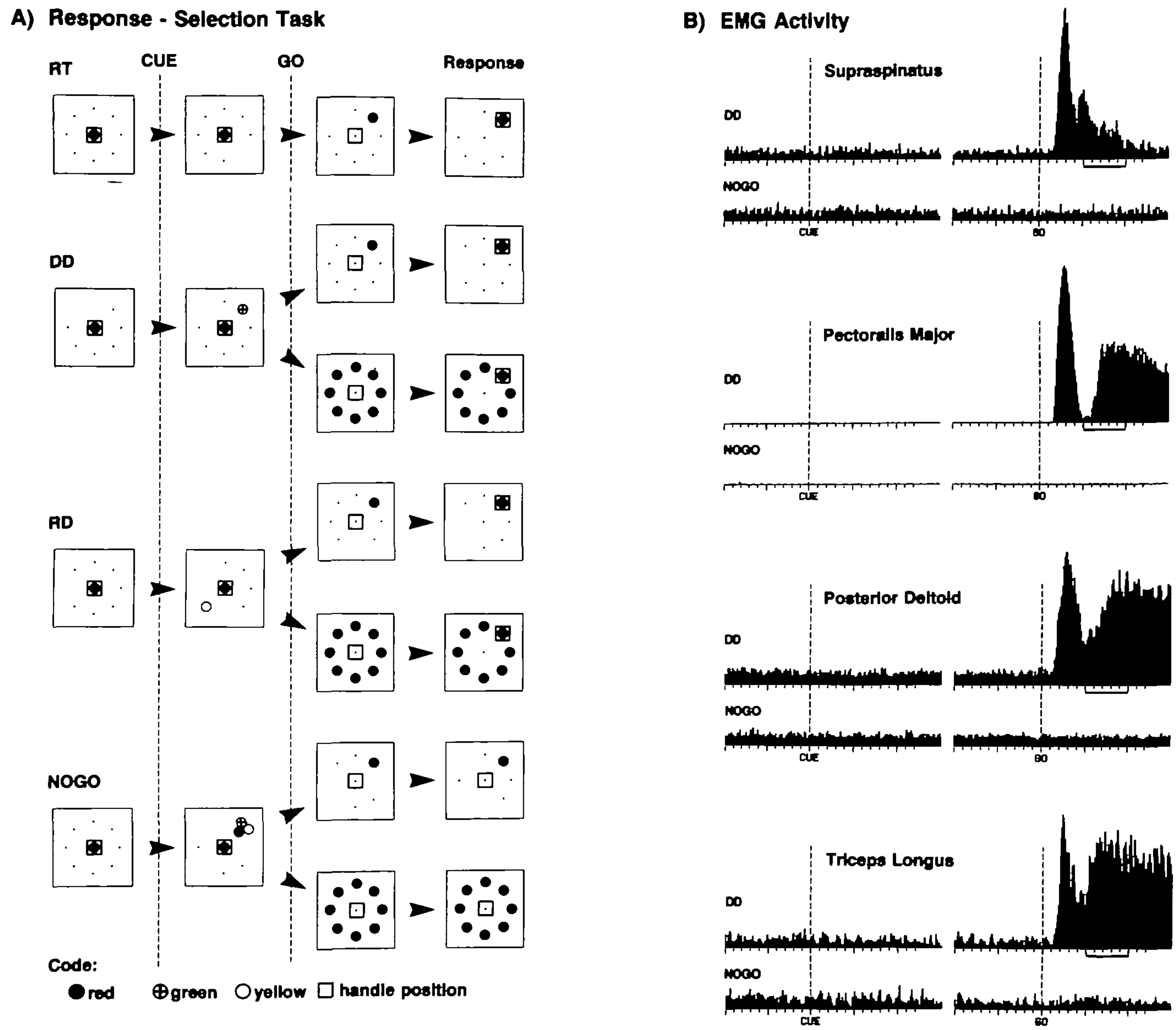

Figure 1. *A*, Schematic representation of the sequence of stimulus events and motor responses for the four trial types in the response-selection task, for one movement direction (in this case, at 45°). Corresponding trials would also be presented at random for the opposite direction (i.e., 225°). Time of presentation of the cue and GO signals is indicated by the *vertical dashed lines*. In the eight-direction task, the monkeys performed only the RT trials and DD trials with spatial GO signals (*top two rows of panels*). *B*, Pairs of histograms showing the contractile activity from selected arm muscles in DD (*upper*) and NOGO (*lower*) trials of the response selection task. Each histogram is the rectified and integrated (10 msec bins) EMG activity summed from 20 trials at the preferred movement direction of the muscle. Data are aligned to the cue and the GO signals (*left and right vertical dashed lines*).

(<250 msec) delay response after the cue at the preferred direction was modestly but significantly stronger than in DD trials ($p < 0.01$, paired t test). Subsequently, the mean premotor population activity in NOGO trials fell rapidly below that in DD trials (second 250 msec and last 500 msec of delay period; $p < 0.01$, paired t test). At the opposite direction, in contrast, the population response was very similar in NOGO and DD trials at all times in the delay period ($p > 0.05$, paired t test). Although the population responses were much more similar at the end of the delay period in the two directions in NOGO trials (mean difference, 3.4 spikes/sec; Fig. 4*A,B*) than in DD trials (mean difference, 15.2 spikes/sec; Fig. 4*A,B*), these differences were still significant for both DD and NOGO trials ($p < 0.01$, paired t test). Furthermore, the mean population response in the last 500 msec of the delay period of NOGO trials was also significantly lower than in RT trials in both directions (RT data not shown; 15.1 spikes/sec vs 18.9 spikes/sec at the preferred direction, 11.7 spikes/sec vs 18.8 spikes/sec at the opposite direction; $p < 0.01$, paired t test). Note also the modest phasic response to the appearance of pseudo-GO signals in NOGO trials in either direction.

In area 5, population activity was strongly directional throughout the delay period of DD and NOGO trials (Fig. 4*C,D*). Furthermore, although there were small differences, at no time was the population response during the delay period of NOGO trials strongly different from that recorded in DD trials in either direction ($p > 0.01$, paired t test).

Single-Cell Responses in Dorsal Premotor Cortex

All 97 selected cells showed changes in discharge during the delay period of DD trials (Figs. 5–7). Most also showed

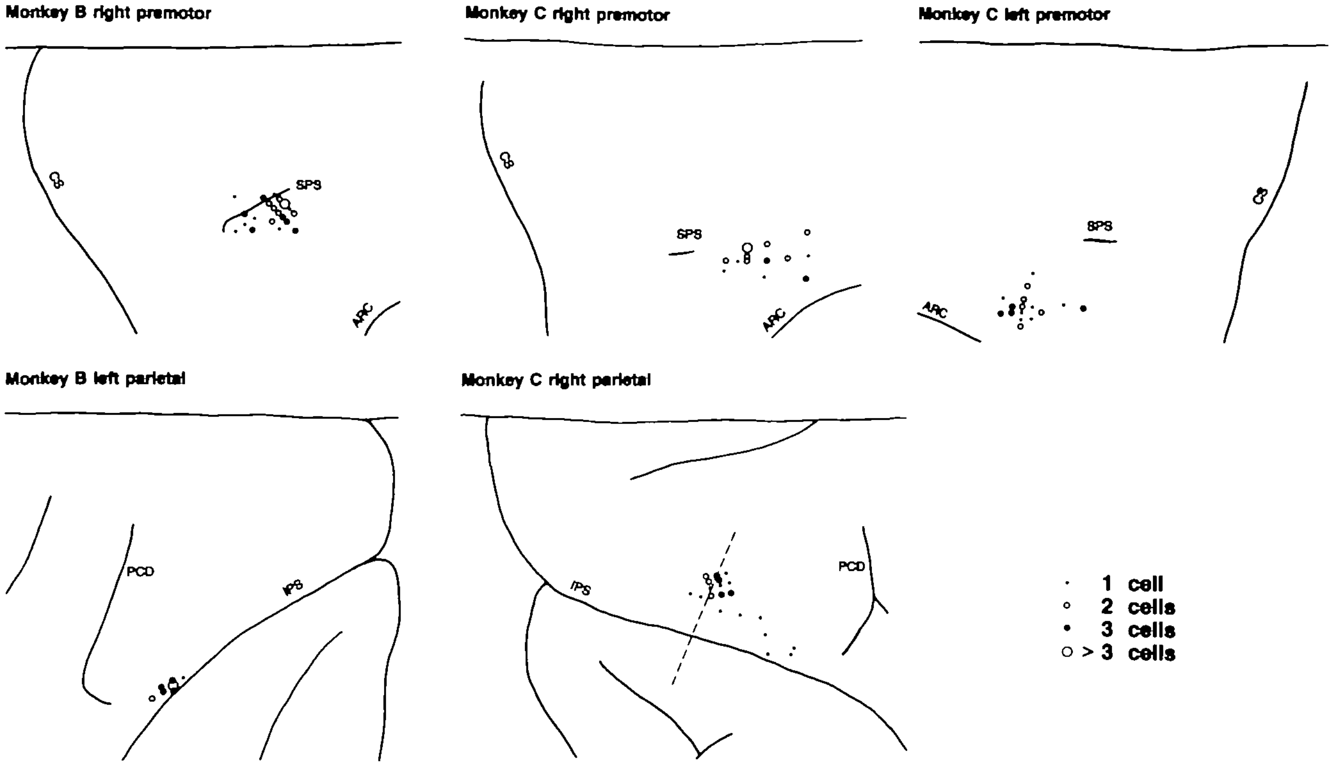

Figure 2. Distribution of the sites of penetrations from which data were collected in the response-selection task in monkeys B and C. *IPS*, intraparietal sulcus; *PCD*, postcentral dimple; *CS*, central sulcus; *SPS*, superior precentral sulcus; *ARC*, arcuate sulcus.

changes in activity during the delay period of NOGO trials, which often also differed from the responses during DD and RT trials. An example of one such premotor neuron is shown in Figure 5. For instance, in the last 500 msec before the GO signal at the preferred direction, the response was significantly stronger in DD trials than in RT trials, but in NOGO trials it was significantly lower (t test, $p < 0.05$). At the opposite direction, cell activity in the last 500 msec of the delay period was significantly lower in both DD and NOGO trials than in RT trials. The responses in DD and NOGO trials were also quite different. The initial activity changes in the first 250 msec after cue presentation were statistically similar in DD and NOGO trials ($p > 0.05$) in both movement directions. However, the responses differed ($p < 0.05$) between the two trial types in the second 250 msec in both directions, and remained different in the last 500 msec at the preferred direction. After the GO signal, there was no modulation in activity in NOGO trials (Fig. 5*E,F*). The directionality of the cell was tested by comparing the activity in the two directions (t test, $p < 0.05$). The cell was not directional at any time prior to the GO signal in RT trials. In contrast, it emitted a directional signal at all times during the delay period of DD trials. In NOGO trials, the cell activity was directional only in the first 250 msec after the cue, and was nondirectional for the rest of the delay period.

In general, most premotor cells showed this pattern of similar initial responses to the cue signals in DD and NOGO trials followed by a progressive divergence of activity. However, the nature of the responses varied widely from cell to cell, with many different combinations of statistical effects in the three delay epochs in the two opposite directions (Figs. 6, 7). As a result, no attempt was made to count cells with specific combinations of responses.

A common response was suppression of tonic activity late in the delay period of NOGO trials below that seen in both RT and DD trials, especially at the preferred direction. This effect was strong in the cell in Figure 6*A–D*, which showed similar initial activity in DD and NOGO trials after the appearance of the cues, in each direction (<250 msec; $p > 0.05$, t test). Later discharge was abruptly suppressed in NOGO trials at the preferred direction (Fig. 6*C*) below that in DD trials (Fig. 6*A*; second 250 msec and last 500 msec, $p < 0.01$). A similar late suppression was also seen in NOGO trials at the opposite direction (Fig. 6*B,D*; $p < 0.01$). In one sense, however, the NOGO responses of such cells at the preferred direction were potentially ambiguous, because their activity also decreased prior to movements in the opposite direction. In contrast, the cell in Figure 6*E–H* showed a strong activity increase during the delay period of DD trials in both directions (Fig. 6*E,F*), but a complete late suppression after the NOGO cues in either spatial location (Fig. 6*G,H*; second 250 msec and last 500 msec, $p < 0.01$).

Some cells showed similar temporal response patterns in both DD and NOGO trials, but the magnitude of the response was less in NOGO trials (Fig. 7*A–D*). At the extreme, the delay period responses of a few cells were almost identical in DD and NOGO trials, so that one could not predict from their discharge whether or not the monkey was going to move. Eight other cells were more active at the end of the delay period of NOGO trials in the preferred direction than in DD trials (Fig. 7*E–H*). All of the latter cells showed a short-latency phasic burst after the onset of the cue signal in the preferred direction in DD trials, followed by a sustained suppression of activity below pre-cue tonic activity (Fig. 7*E*). In NOGO trials at the same direction (Fig. 7*G*), the cue evoked a similar short-latency burst, followed in that particular cell by a brief suppression and a subsequent rebound above pre-cue levels for the remainder of the delay period. The other seven cells emitted sustained activity after the initial phasic burst, without the transient suppression.

Figure 3. Photomontage of two adjacent histological sections through the intraparietal sulcus of monkey C, with a series of lesions (*arrows a–c*) marking a penetration in which area 5 cells with complex NOGO responses (Figs. 13–15) were recorded between lesions *b* and *c*. The *open arrows* mark the path of an adjacent electrode trajectory. Approximate plane of section is indicated by the dashed line in the corresponding cortical map (Fig. 2, lower center). *IPS,* intraparietal sulcus; *STS,* superior temporal sulcus. Scale bar, 1 mm

Single-Cell Responses in Parietal Area 5

Area 5 cells also showed changes in activity during the delay period of both DD trials and NOGO trials. However, their DD and NOGO delay activity was often similar, and did not show the wide range of patterns seen in premotor cells. Figure 8 illustrates an area 5 neuron that emitted strong sustained discharges throughout the ID period of DD and NOGO trials at the preferred direction and a suppression at the opposite direction. Quantitatively, the response was stronger in the first and second 250 msec after cues at the preferred direction in NOGO trials than in DD trials (t test, $p < 0.05$), but similar in the last 500 msec before the GO signal ($p > 0.05$). At the opposite direction, the cell's activity was indistinguishable between DD and NOGO trials at all times after cue presentation ($p > 0.05$). The cell was directional throughout the delay period of both trial types (t test, $p < 0.05$).

Figure 9 illustrates a second area 5 cell with similar properties. The only difference in delay activity between DD and NOGO trials occurred in the second 250 msec after the cue at the opposite direction, when the NOGO activity was modestly but significantly weaker ($p < 0.05$).

Quantitative Comparison of Delay Period Activity between Premotor Cortex and Area 5

Table 1 is a compilation of the statistical comparisons ($p < 0.05$, t test) of the mean discharge of single cells at different times during the delay period of DD and NOGO trials.

First, cells were tested for differences in activity between DD and RT trials (Table 1*Ai,Bi*). There was a significant increase (χ^2 test, $p < 0.01$) in the number of premotor and area 5 cells that showed a differential response in DD versus RT trials at the preferred direction as the delay period progressed, in particular in the number of cells that were more active in DD trials. At the opposite direction, there was a reciprocal significant increase in the number of cells that were less active in DD than RT trials throughout the delay period.

Second, cells were tested for a differential response between NOGO and RT trials (Table 1*Aii,Bii*). Area 5 cells again showed reciprocal significant increases in the number of cells that were more or less active in NOGO trials than in RT trials throughout the delay period in the two movement directions (Table 1*Bii*), similar to that seen in DD trials (Table 1*Bi*). The premotor cells behaved differently (Table 1*Aii*). At the pre-

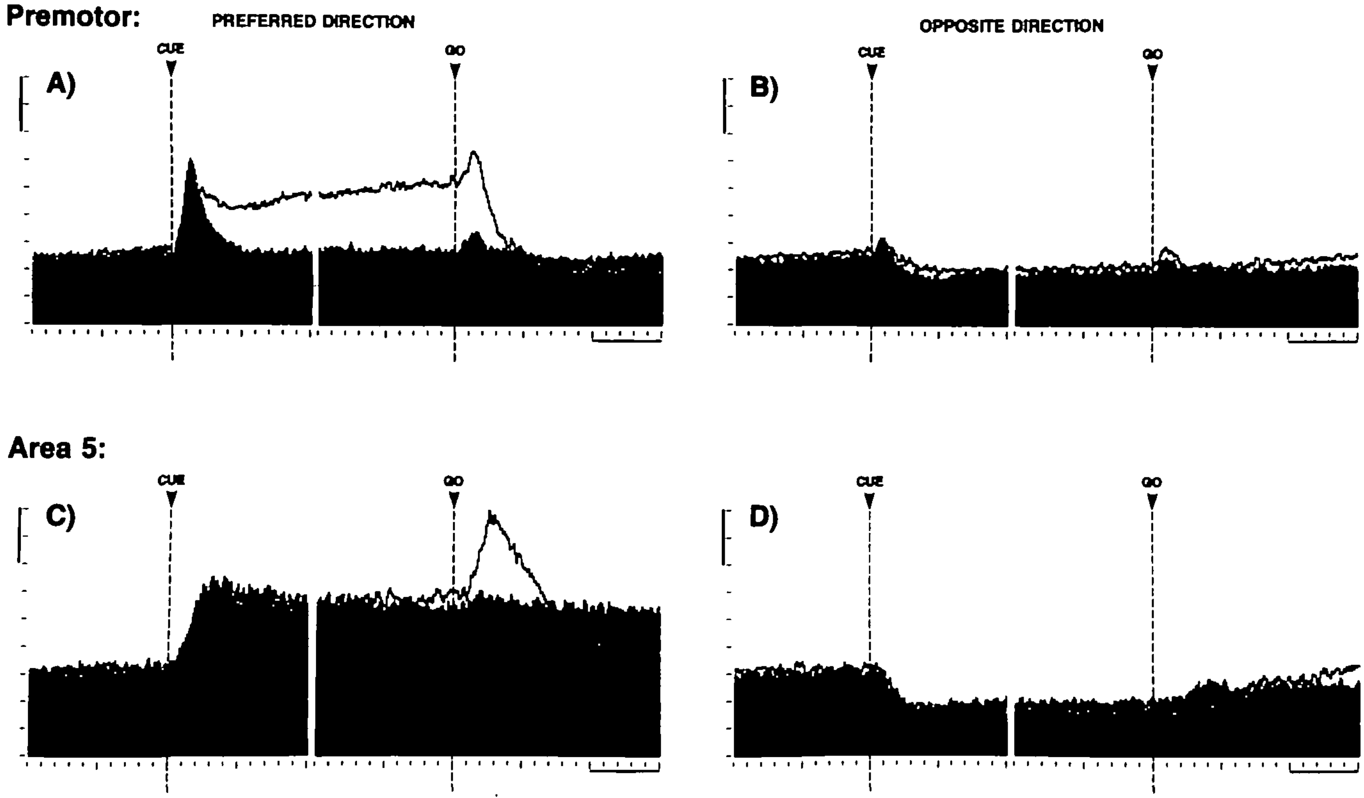

Figure 4. Population histograms of the mean response of the premotor cortex (*A*, *B*) and area 5 (*C*, *D*) sample populations during DD (*outlined histograms*) and NOGO (*solid histograms*) trials in opposite directions. Calibration for this and all subsequent figures (except where indicated): 500 msec, 10 spikes/sec.

ferred direction, there was a significant decline in the number of cells whose discharge was greater in NOGO trials than in RT trials and a progressive increase in the number of cells whose activity was equal to or less than that in RT trials (Table 1*Aii*; $p < 0.01$, χ^2 test). In contrast, at the opposite direction, the comparisons between NOGO and RT trials (Table 1*Aii*) showed the same distribution of results throughout the delay period as that seen for DD trials (Table 1*Ai*; $p > 0.05$, χ^2 test).

Next, the delay period activity was compared directly between DD and NOGO trials (Table 1*Aiii,Biii*). In the first 250 msec after cue appearance in both directions, the large majority of cells in both premotor cortex and area 5 showed similar activity in DD and NOGO trials. For the remainder of the delay period, there was a progressive decline in the number of cells with similar responses in DD and NOGO trials, in both directions. However, this decline was significantly sharper in premotor cortex than in area 5, and more evident in the preferred direction ($p < 0.01$, χ^2 test for second 250 msec and last 500 msec) than in the opposite direction ($p < 0.01$, χ^2 test, last 500 msec only).

A different question concerns whether cell responses were significantly different in the two directions ($p < 0.05$, t test), and whether the degree of directionality differed between trial types (Table 2). In DD trials in both regions, the number of directionally tuned cells increased significantly throughout the delay period (χ^2 test, $p < 0.01$). In NOGO trials, there was also an increase in the number of directionally tuned cells throughout the delay period in area 5 (Table 2*B*; χ^2 test, $p < 0.01$), but not in premotor cortex (Table 2*A*; $p > 0.05$, χ^2 test). In both areas, the number of directional cells was similar between DD and NOGO trials in the first and second 250 msec of the delay period ($p > 0.05$, χ^2 test), but fewer in the last 500 msec period in NOGO trials than in DD trials (Table 2*A*, $p < 0.01$, χ^2 test; Table 2*B*, $p < 0.025$, χ^2 test). Finally, whereas the majority of cells were directionally tuned during the delay period of NOGO trials, they were equally common in both populations only in the first 250 msec after cue appearance ($p > 0.05$, χ^2 test), but significantly fewer in the premotor cortex than in area 5 in the rest of the delay period ($p < 0.025$, χ^2 test).

The effect of the DD and NOGO instructions on the mean activity of cells was further compared using a correlation analysis (Fig. 10). Premotor responses in the two trial types were strongly correlated in the first 250 msec of the delay period (Fig. 10*A*; $r = 0.94$). Thereafter, there was a much greater variation in the responses of the cells between DD and NOGO trials ($r = 0.67$, Fig. 10*B*; $r = 0.57$, Fig. 10*C*), and most data points lay below the identity line, indicating higher levels of activity in DD trials (Table 1*Aiii*). A similar decline in correlation occurred at the opposite direction (data not shown; $r = 0.93$, 0.70, and 0.69 in the three successive epochs), but a strong shift away from the identity line was not seen (Table 1*Aiii*).

In contrast, area 5 cell responses showed much less variation between DD and NOGO trials across the three delay epochs ($r = 0.96$, Fig. 10*D*; $r = 0.87$, Fig. 10*E*; $r = 0.81$, Fig. 10*F*). Moreover, there was no strong shift of the distribution from the identity line. Similar results were found for area 5 cells at the opposite direction (data not shown; $r = 0.95$, 0.87, and 0.87 in the three successive delay period epochs).

Activity Changes after Pseudo-GO Signals in NOGO Trials: "Sensory" or "Motor"?

The monkeys were carefully trained to make no overt motor responses to the instructional signals in DD and NOGO trials,

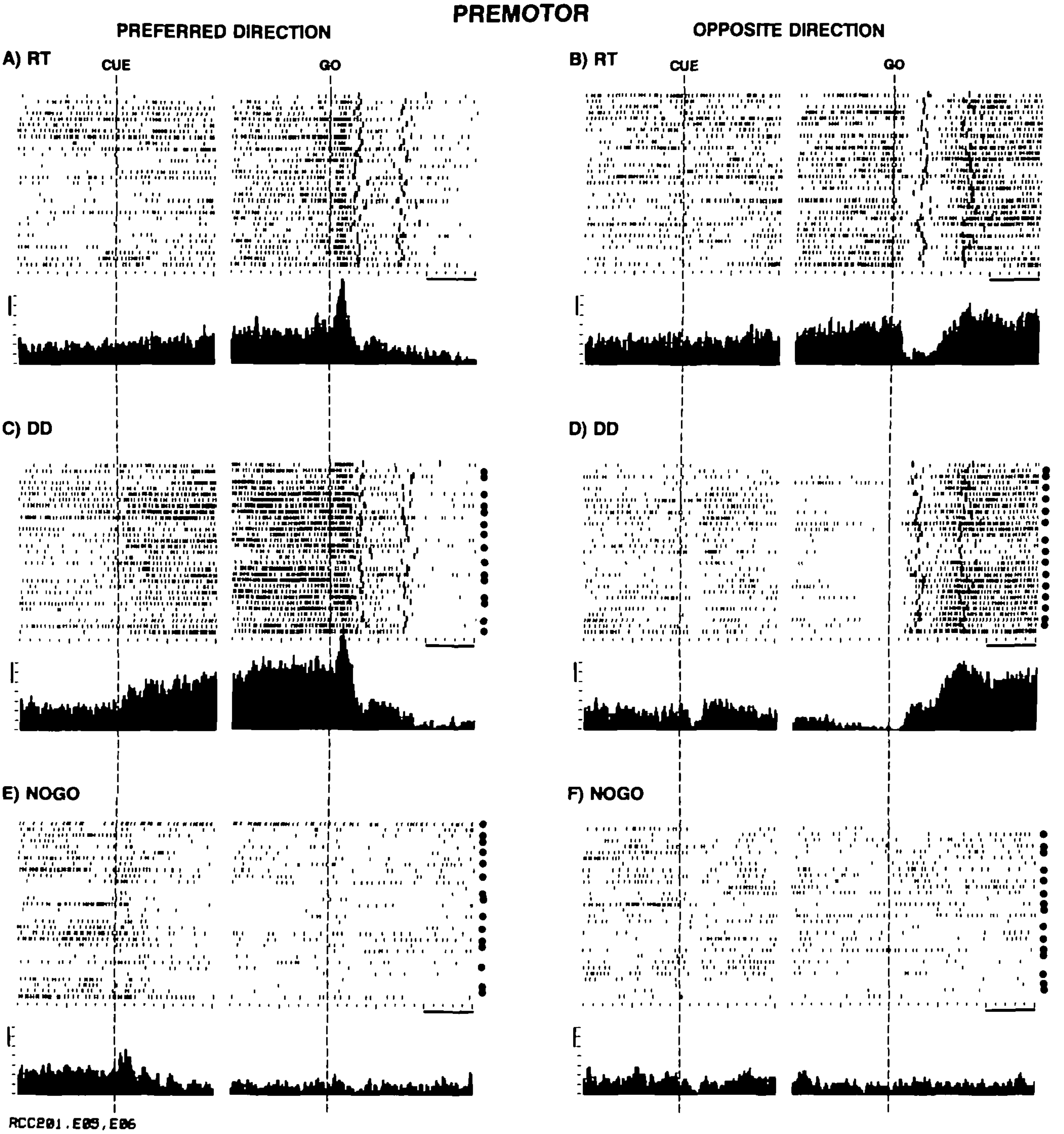

Figure 5. Raster and histogram representation of the responses of a premotor neuron for two opposite movement directions in the task. *A* and *B*, Reaction-time trials with no cue presented. *C* and *D*, Direct delay trials. *E* and *F*, NOGO trials. The *two thick markers* to the right of GO in each raster line indicate, respectively, the time of the onset and end of movement toward the target. *Black dots* to the right of raster lines indicate catch trials with nonspatial GO signals.

and EMG recordings confirmed the lack of activity in prime-mover muscles after presentation of the pseudo-GO signals (Fig. 1*B*). Nonetheless, many cells showed responses to the pseudo-GO signals. A striking example in an area 5 cell is shown in Figure 9, recorded in monkey C. In NOGO trials at the opposite direction, cell activity remained suppressed after presentation of the spatially matched GO signal, whereas a tonic discharge occurred after the nonspatial pseudo-GO signal of catch trials (Fig. 9*D*, trials indicated by dots), suggesting a visual response to the illumination of LEDs at the preferred direction. A corresponding effect was not seen in NOGO trials at the preferred direction (Fig. 9*C*).

To investigate further the post-GO responses in NOGO trials, that cell was tested in a modified NOGO task using spatially patterned pseudo-GO signals (Fig. 11). As before, NOGO cues at the opposite direction (90°, Fig. 11*B*) suppressed activity throughout the delay period. Whenever the LED at 270° was illuminated as part of the patterned pseudo-GO signal,

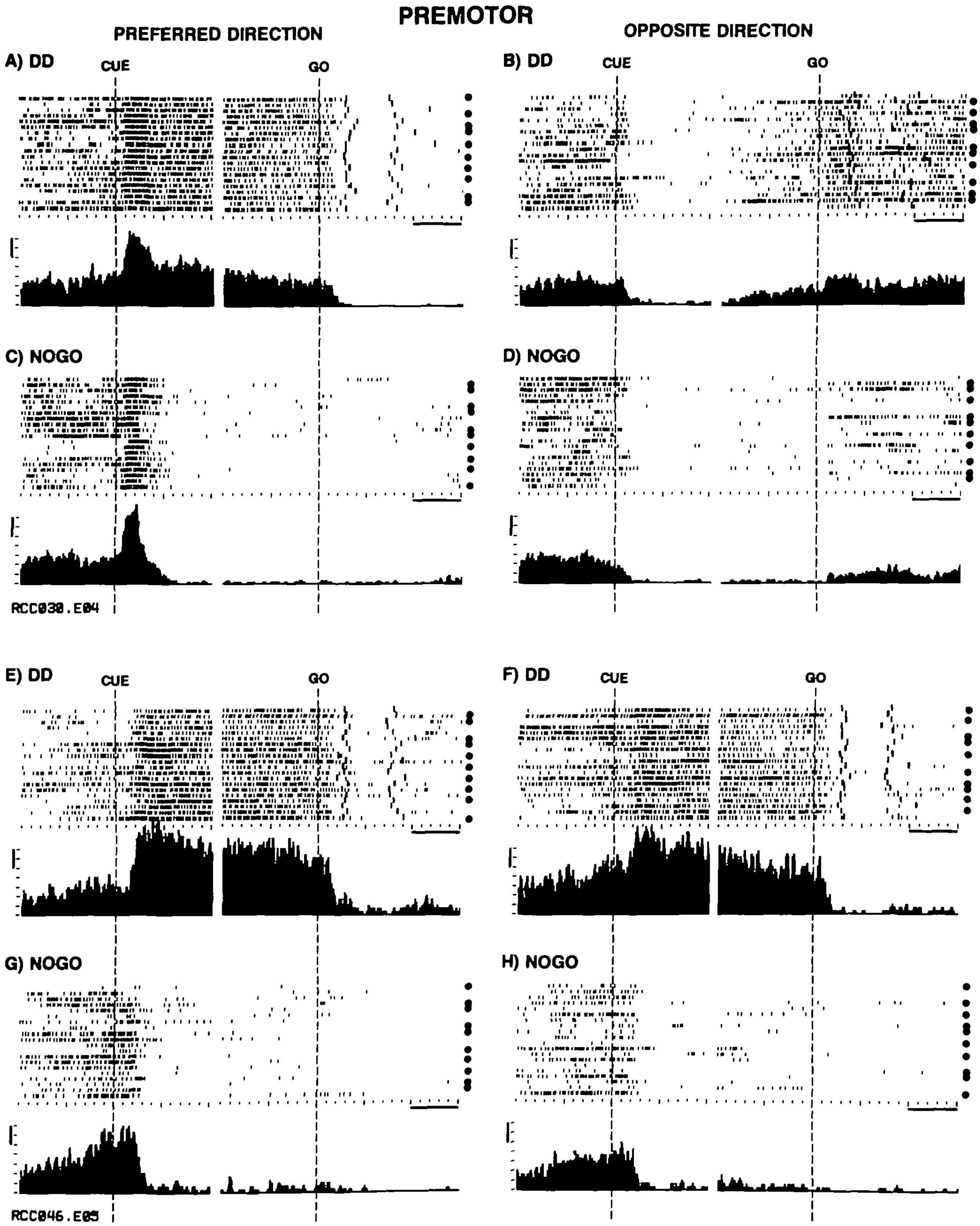

Figure 6. Raster and histogram representations of the responses of two premotor neurons (*A–D, E–H*) during DD and NOGO trials in two opposite directions. Vertical calibration in *A–D*, 20 spikes/sec.

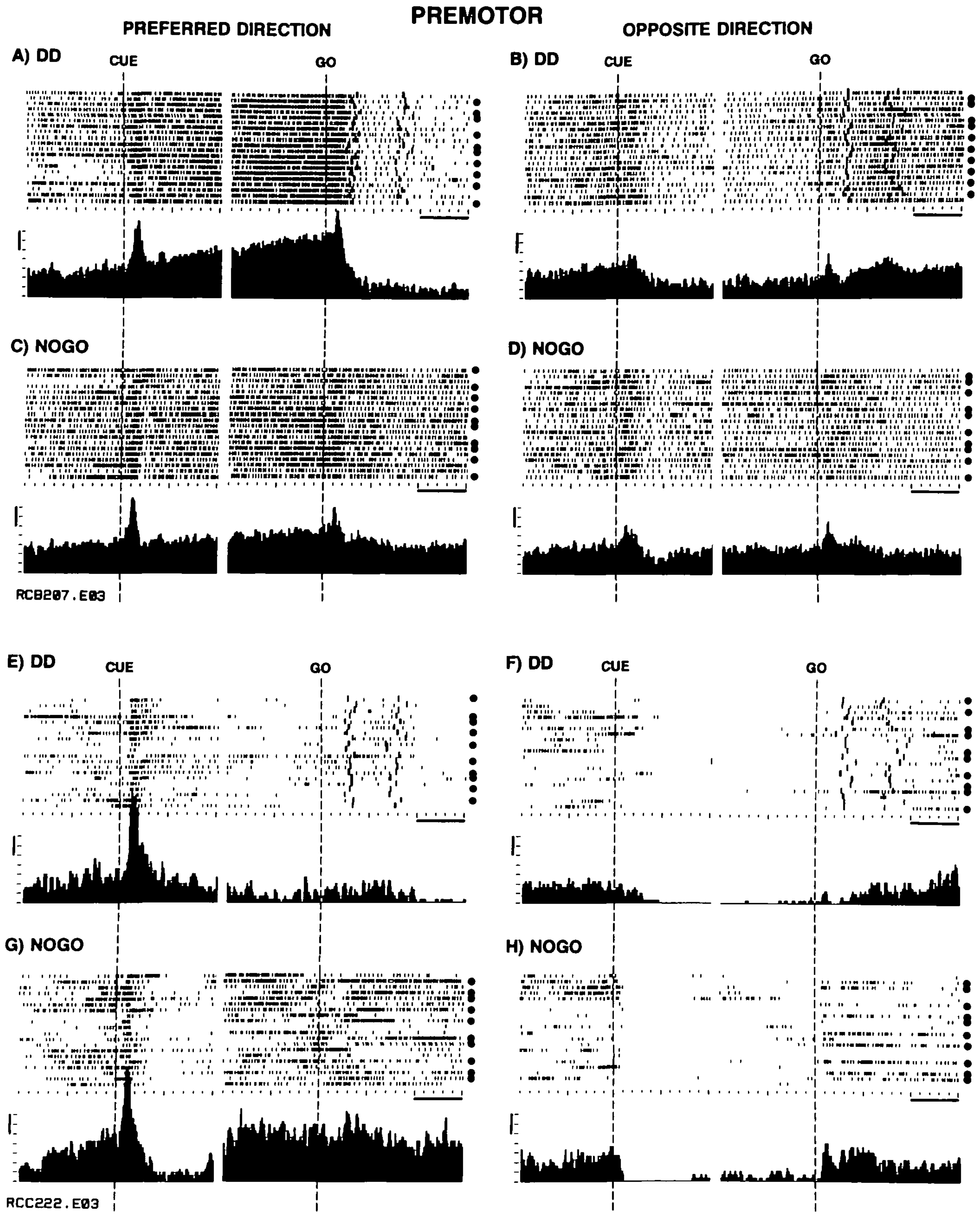

Figure 7. Raster and histogram representations of the responses of two premotor neurons (*A–D, E–H*) during DD and NOGO trials in two opposite directions. Vertical calibration in *A–D*, 20 spikes/sec.

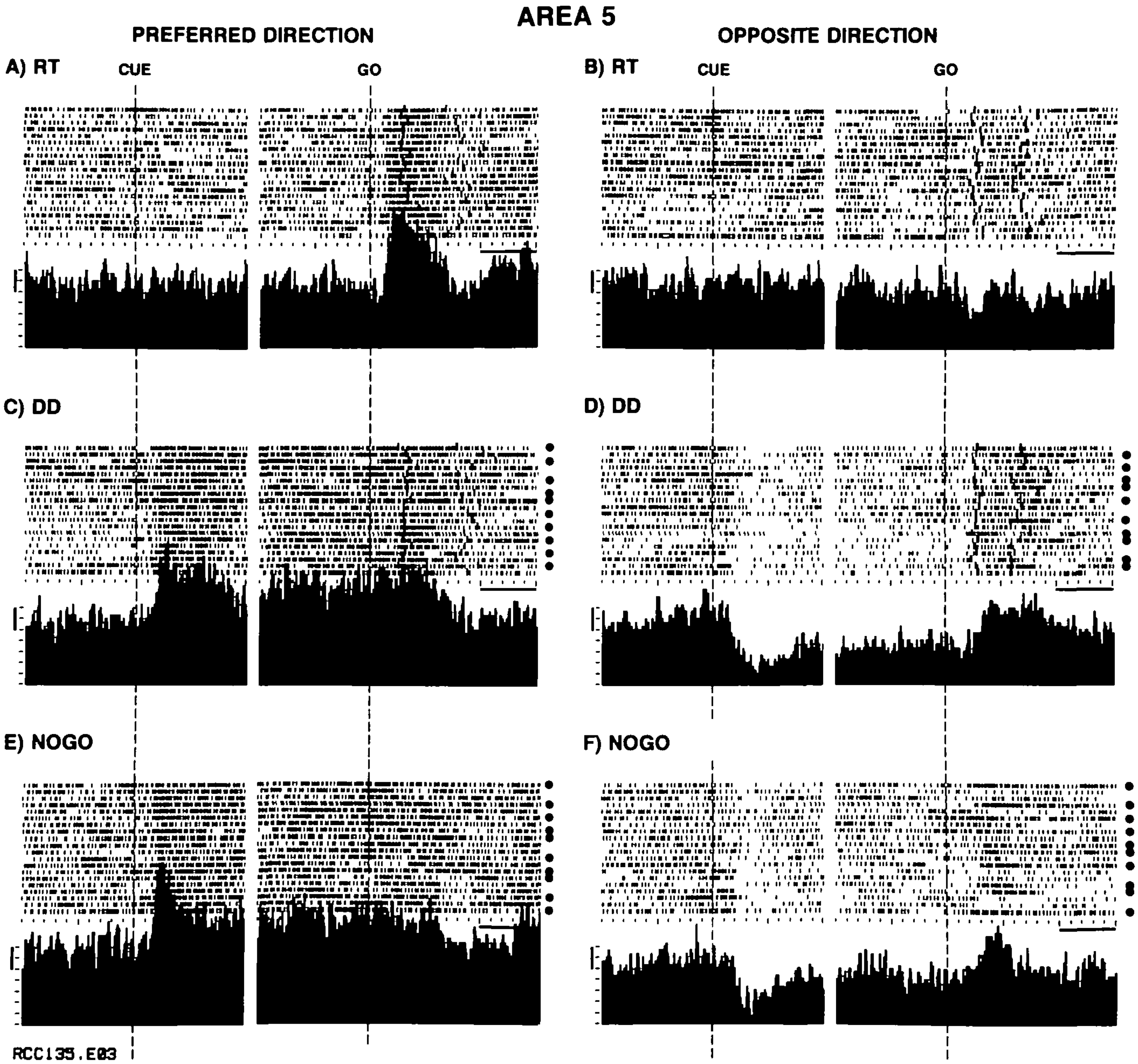

Figure 8. Raster and histogram representations of the responses of an area 5 neuron during RT (*A, B*), DD (*C, D*), and NOGO trials (*E, F*) in two opposite directions.

the cell showed an abrupt increase in activity (Fig. 11*B*, lower five rasters). In contrast, NOGO cues at the preferred direction (270°, Fig. 11*A*) activated the cell in the delay period and this activity persisted as long as the target at 270° remained on as part of the patterned GO signal (Fig. 11*A*, lower five rasters). The specificity of this effect is striking, as shown by the rasters (Fig. 11*A,B*, third raster from top) recorded when all seven LEDs other than at 270° were illuminated as the GO signal and the cell was strongly suppressed, whether or not the preceding NOGO cue activated or suppressed the cell. Finally, the cell was activated when all eight LEDs were illuminated (Fig. 11*A,B*, fourth raster from top), indicating that the suppressive influence of the LED at 90° was masked by the concurrent activation evoked by the LED at 270°.

The modulations in activity in Figure 11 occurred as the monkey held its arm over the central target while LEDs were turned on and off, as if the cell was responding passively to the presentation of visual stimuli. Other evidence argues against that possibility. First, when that cell was tested in the MEM task (Fig. 12), sustained increases and decreases in tonic activity after extinction of the cues in MEM trials at the preferred and opposite directions (Fig. 12*C,D*) showed that the continued presence of the visual stimuli was not necessary to sustain the response. Second, the presence of the stimuli was not always sufficient to evoke a response, since all of the trials in Figure 12 used nonspatial catch GO signals yet no tonic rebound was recorded after the GO signal was illuminated at the opposite direction [Fig. 12*B,D*; see also catch DD trials (dots) in Fig. 9*B*]. Therefore, whenever the monkey intended to move, the activity of the cell paralleled the motor instructional content of the cues, even when they were removed or replaced by nonspatial GO signals.

The cell in Figures 9 and 11 did not respond to passive manipulation of the arm or body, or to passive visual stimuli

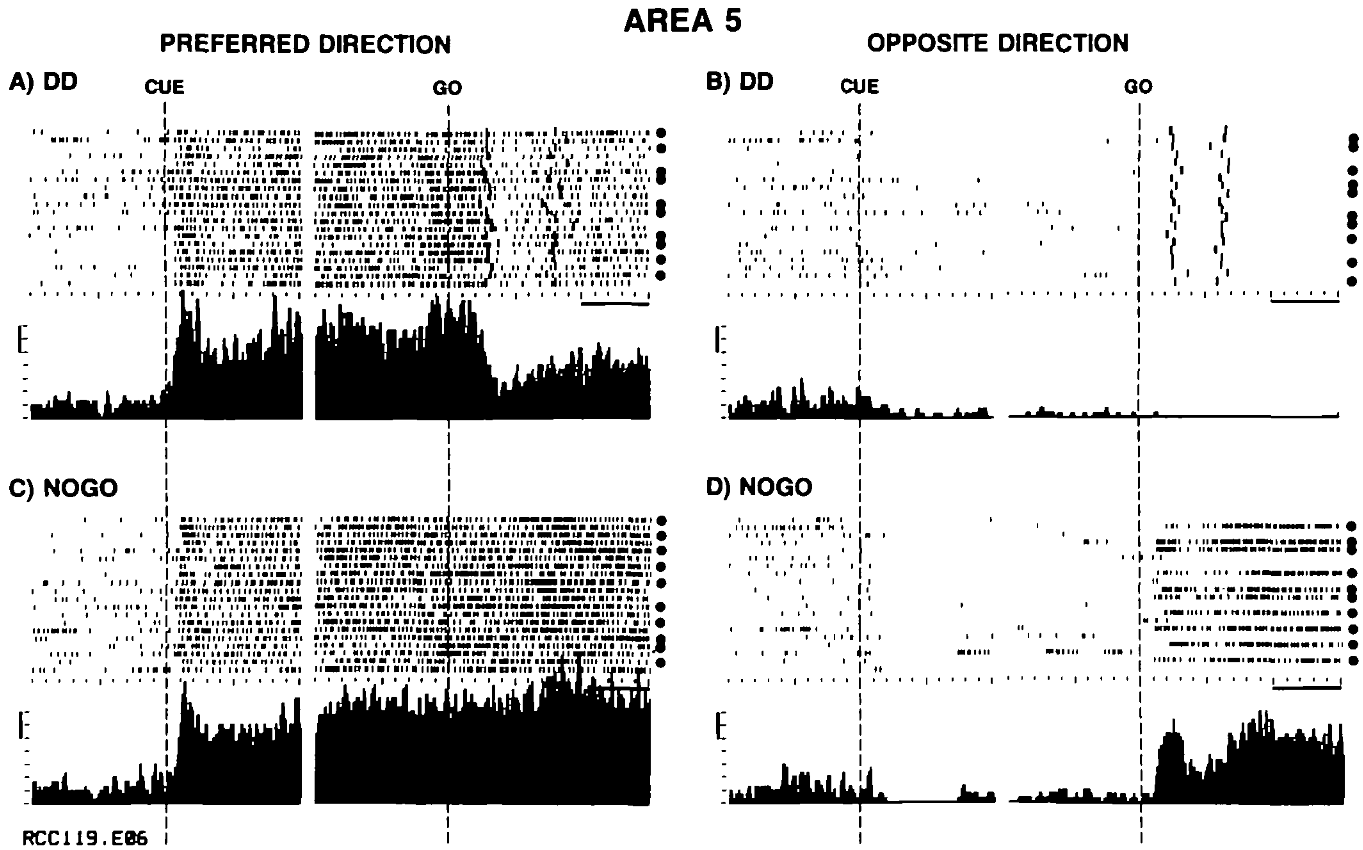

Figure 9. Raster and histogram representations of the responses of an area 5 neuron during DD and NOGO trials in two opposite directions.

presented outside of the task, but discharged during reaching movements for raisins. Moreover, when the monkey's arm was held gently over the central target and a raisin was placed over the LED at 270°, the cell emitted a strong tonic discharge, recapitulating its activity in the task. The tonic activity ceased when the arm was then moved passively behind the monkey's back, suggesting that it depended on the relative location of the arm and raisin.

Six other area 5 cells tested with the modified NOGO task of Figure 11 behaved similarly. A further 12 cells showed the post-GO modulation in NOGO catch trials but were not tested in the NOGO task of Figure 11. In all cases, one of the two opposite cue locations along the cell's preferred-direction axis was dominant in that when all eight LEDs were illuminated, its effect on cell activity, whether excitatory or inhibitory, masked that of the LED at the opposite cue location. Interestingly, in 17 of 19 cells, the dominant target was at the location along the cell's preferred direction axis that was closest to the body, and not necessarily the target that was at the cell's preferred direction. This suggests a strong spatial dependence on the nature of a cell's response to simultaneous presentation of targets in different locations.

The behavior of a different cell from monkey C (Figs. 13–

Table 1
Comparison of delay period responses in different trial types

		Preferred direction			Opposite direction		
		1st 250 msec	2d 250 msec	last 500 msec	1st 250 msec	2d 250 msec	last 500 msec
A. Premotor (n = 97 cells)							
i.	DD > RT	47 (48.5%)	52 (53.6%)	60 (61.8%)	9 (9.3%)	7 (7.2%)	14 (14.4%)
	DD < RT	4 (4.1%)	8 (8.2%)	10 (10.3%)	17 (17.5%)	42 (43.3%)	62 (63.9%)
	DD = RT	46 (47.4%)	37 (38.1%)	27 (27.8%)	71 (73.2%)	48 (49.5%)	21 (21.6%)
ii.	NOGO > RT	51 (52.6%)	33 (34.0%)	9 (9.3%)	12 (12.4%)	12 (12.4%)	7 (7.2%)
	NOGO < RT	7 (7.2%)	21 (21.6%)	39 (40.2%)	23 (23.7%)	51 (52.6%)	62 (63.9%)
	NOGO = RT	39 (40.2%)	43 (44.3%)	49 (50.5%)	62 (63.9%)	34 (35.1%)	28 (28.9%)
iii.	DD > NOGO	4 (4.1%)	40 (41.2%)	70 (72.2%)	9 (9.3%)	21 (21.6%)	24 (24.7%)
	DD < NOGO	14 (14.4%)	3 (3.1%)	8 (8.3%)	4 (4.1%)	11 (11.3%)	27 (27.8%)
	DD = NOGO	79 (81.4%)	54 (55.7%)	19 (19.6%)	84 (86.6%)	65 (67.0%)	46 (47.4%)
B. Area 5 (n = 47 cells)							
i.	DD > RT	16 (34.0%)	33 (70.2%)	36 (76.6%)	0 (0.0%)	0 (0.0%)	1 (2.1%)
	DD < RT	0 (0.0%)	0 (0.0%)	1 (2.1%)	7 (14.9%)	29 (61.7%)	33 (70.2%)
	DD = RT	31 (66.0%)	14 (29.8%)	10 (21.3%)	40 (85.1%)	18 (38.3%)	13 (27.7%)
ii.	NOGO > RT	20 (42.6%)	37 (78.7%)	31 (66.0%)	0 (0.0%)	2 (4.3%)	1 (2.1%)
	NOGO < RT	1 (2.1%)	0 (0.0%)	2 (4.3%)	9 (19.1%)	30 (63.8%)	30 (63.8%)
	NOGO = RT	26 (55.3%)	10 (21.3%)	14 (29.8%)	38 (80.9%)	15 (31.9%)	16 (34.0%)
iii.	DD > NOGO	1 (2.1%)	5 (10.6%)	16 (34.0%)	2 (4.3%)	7 (14.9%)	3 (6.4%)
	DD < NOGO	4 (8.5%)	9 (19.1%)	6 (12.8%)	0 (0.0%)	5 (10.6%)	9 (19.1%)
	DD = NOGO	42 (89.4%)	33 (70.2%)	25 (53.2%)	45 (95.7%)	35 (74.5%)	35 (74.5%)

Table 2
Cells with directionally tuned delay period activity

	1st 250 msec	2d 250 msec	last 500 msec
A. Premotor (n = 97 cells)			
RT	1 (1.0%)	5 (5.2%)	2 (2.1%)
DD	58 (59.8%)	78 (80.4%)	84 (86.6%)
NOGO	65 (67.0%)	68 (70.1%)	59 (60.8%)
B. Area 5 (n = 47 cells)			
RT	3 (6.4%)	1 (2.1%)	1 (2.1%)
DD	24 (51.1%)	43 (91.5%)	45 (95.7%)
NOGO	28 (59.6%)	42 (89.4%)	38 (80.9%)

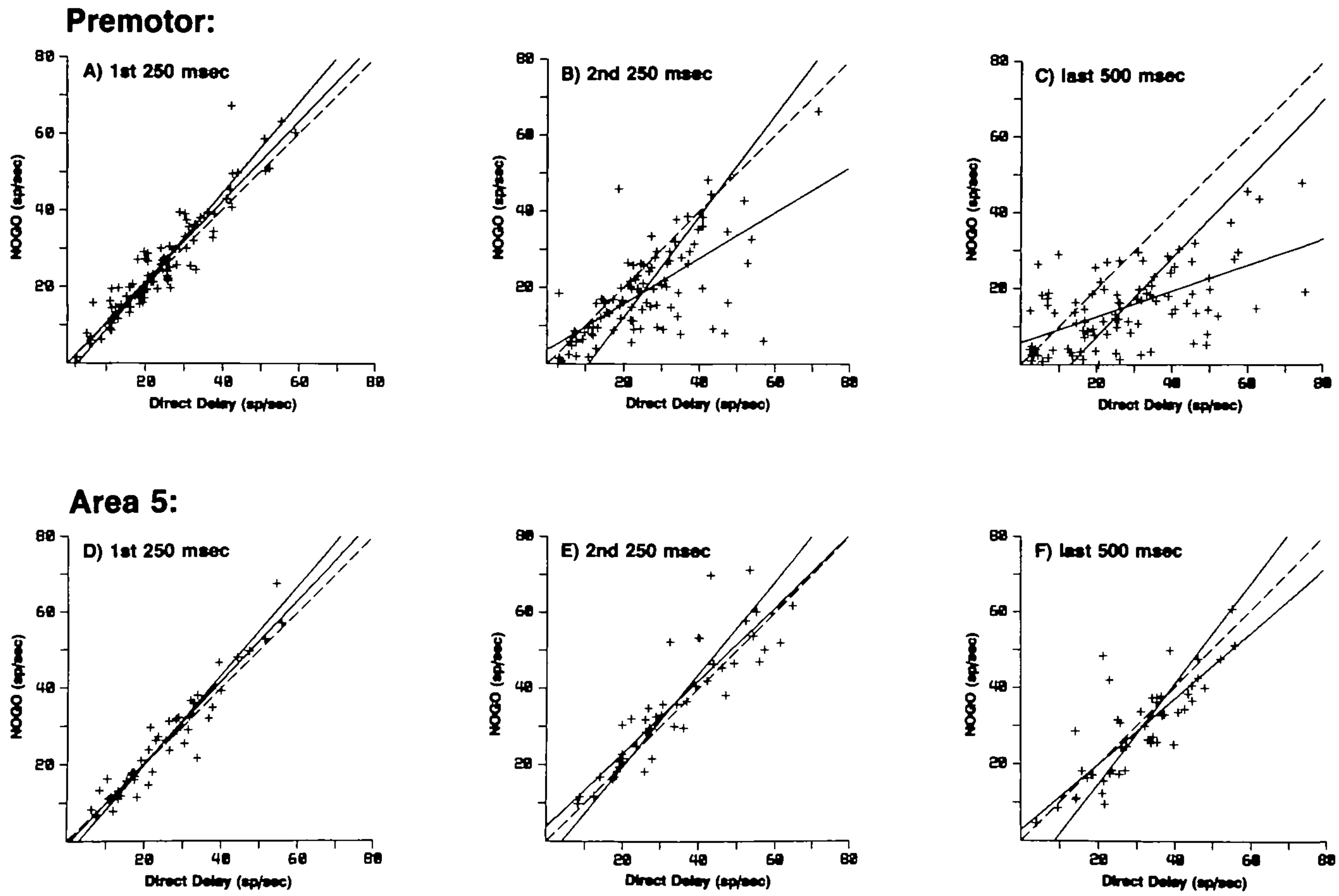

Figure 10. Scatter plots of the mean response of premotor (*A–C*) and area 5 cells (*D–F*) at different times in the delay period of DD and NOGO trials. The *diagonal dashed lines* are the identity line, and the *solid lines* are the regression lines for abscissa on ordinate and ordinate on abscissa.

15) further reveals how the directional tuning of area 5 activity better reflects potential motor responses than stimulus locations. The cell, recorded at lesion site b in Figure 3, showed a post-GO decrease of activity in NOGO catch trials at the preferred direction (Fig. 13*C*) but no modulation at the opposite direction (Fig. 13*D*). The cell was then tested in a modified NOGO task using spatially nonmatched pseudo-GO signals (Fig. 14), which produced tonic post-GO responses whose intensity varied as a function of the spatial location of the pseudo-GO signals. The directional tuning of the post-GO activity was very similar whether the NOGO cue appeared at the cell's preferred direction (Figs. 14*A*, 15*C*, solid lines) or in the opposite direction (Figs. 14*B*, 15*D*, solid lines). It was also strikingly similar to the response of the cell during the delay and movement epochs of DD trials collected in the eight-direction task (Fig. 15*A*,*B*, dashed and solid lines). Therefore, the directional tuning of the cell when the monkey intended to make a movement toward the spatial location of the DD cues and the response of the neuron to the pseudo-GO signals in the modified NOGO task were similar. Five other cells tested in the NOGO task of Figure 14 likewise responded to the single-LED pseudo-GO signals with continually graded modulations in activity whose directionality resembled that in DD trials of the eight-direction task.

The possibility that this was a simple passive response to the location of visual stimuli was again refuted by other evidence. As was the case for many premotor and area 5 cells, the cell in Figure 13 was active and directionally tuned when the monkey performed the task with either arm (Crammond and Kalaska, 1991, unpublished observations). However, the directional tuning of this particular cell in the eight-direction task was very different while the monkey used the different arms (Fig. 15*B*,*E*), as if it was signaling how to acquire the targets with the two arms rather than their spatial locations per se. The cell responses in the modified NOGO task were also quite different with the two arms. NOGO cues at 90° and at 270° did not evoke the large changes in tonic activity during the delay period when working with the ipsilateral arm (Fig. 15*F*,*G*, dashed lines) as occurred with the contralateral arm (Fig. 15*C*,*D*, dashed lines). Likewise, the responses evoked by the pseudo-GO cues were quite different while the monkey held the handle over the central target with the ipsilateral arm (Fig. 15*F*,*G*, solid lines) and contralateral arm (Fig. 15*C*,*D*, solid lines). This cell did not have a passive somatic receptive field or visual driving, but discharged during reaching movements with either arm outside of the task with the same directionality as seen in the corresponding DD trials (Fig. 15*B*,*E*).

Responses to pseudo-GO signals in NOGO trials were seen in both monkeys but were more prominent in monkey C and located in a part of area 5 more medial and deep to the region that we normally study posterior to the postcentral dimple (Figs. 2, 3; Kalaska et al., 1990). Nevertheless, area 5 cells in both monkeys showed similar sustained delay-period responses in DD and NOGO trials, irrespective of how they behaved after the GO signals.

Many premotor cells also showed post-GO responses in NOGO trials, with equal probability in premotor (52 of 97) and parietal cortex (26 of 47; $p > 0.05$, χ^2 test), and with equal probability at the preferred and opposite directions (39

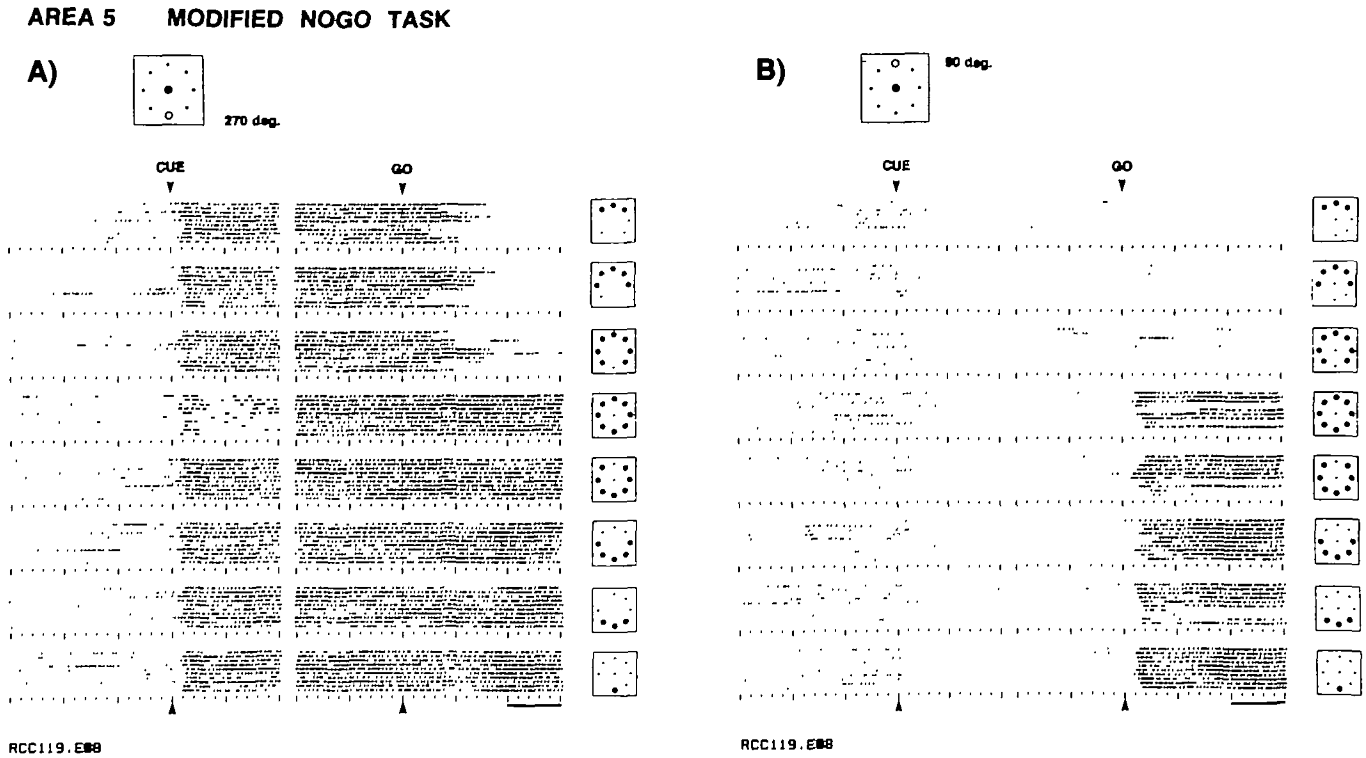

Figure 11. Raster representations of the responses of the cell in Figure 9 during a modified NOGO task. NOGO cues were presented at 270° (*A*) or at 90° (*B*). *Target panel replicas* to the right of each raster show the combination of LEDs illuminated as pseudo-GO signals.

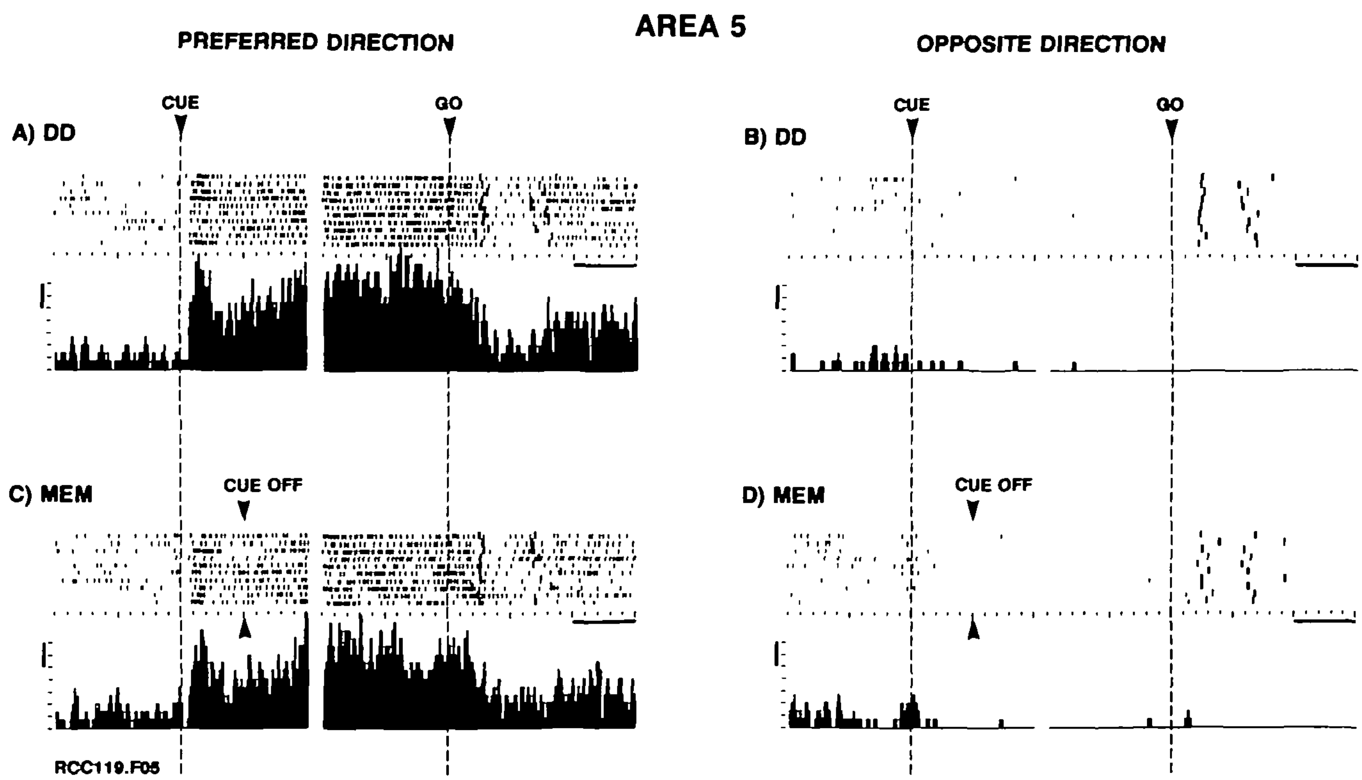

Figure 12. Raster and histogram representations of the responses of the cell in Figure 9 in DD (*A*, *B*) and MEM (*C*, *D*) trials in opposite directions.

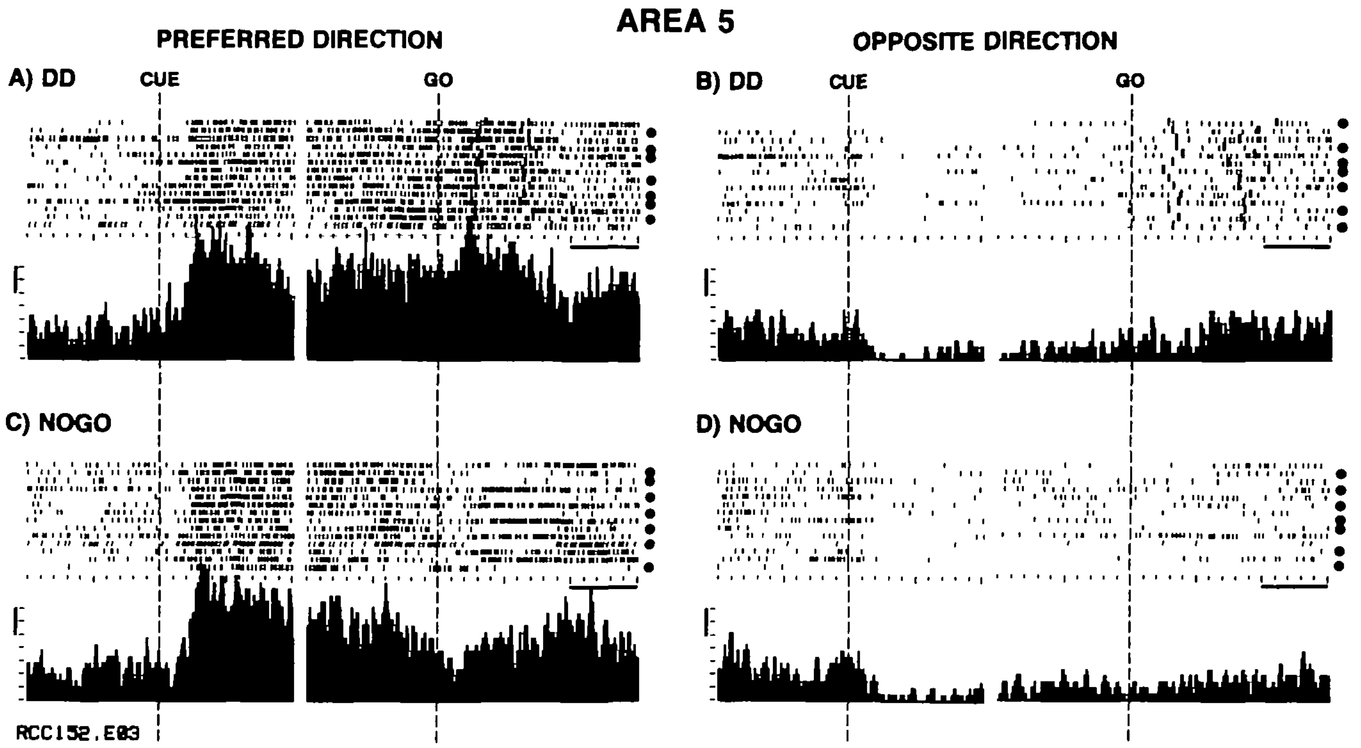

Figure 13. Raster and histogram representations of the responses of an area 5 neuron during DD and NOGO trials in two opposite directions. This cell was recorded at lesion site b in Figure 3.

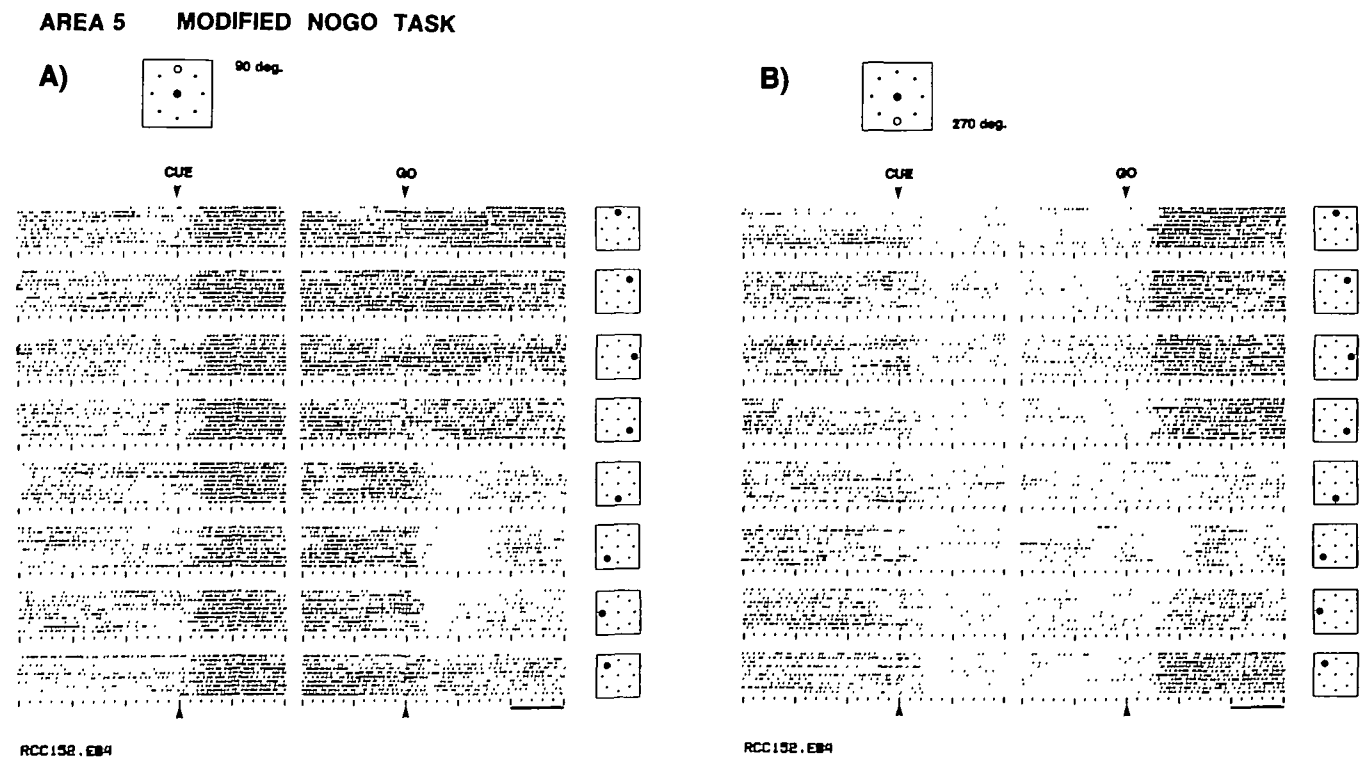

Figure 14. Raster representations of the responses of the cell in Figure 13 during a modified NOGO task. NOGO cues were presented at 90° (*A*) and at 270° (*B*). *Target panel replicas* to the right of each raster indicate the location of the LED illuminated as the pseudo-GO signal.

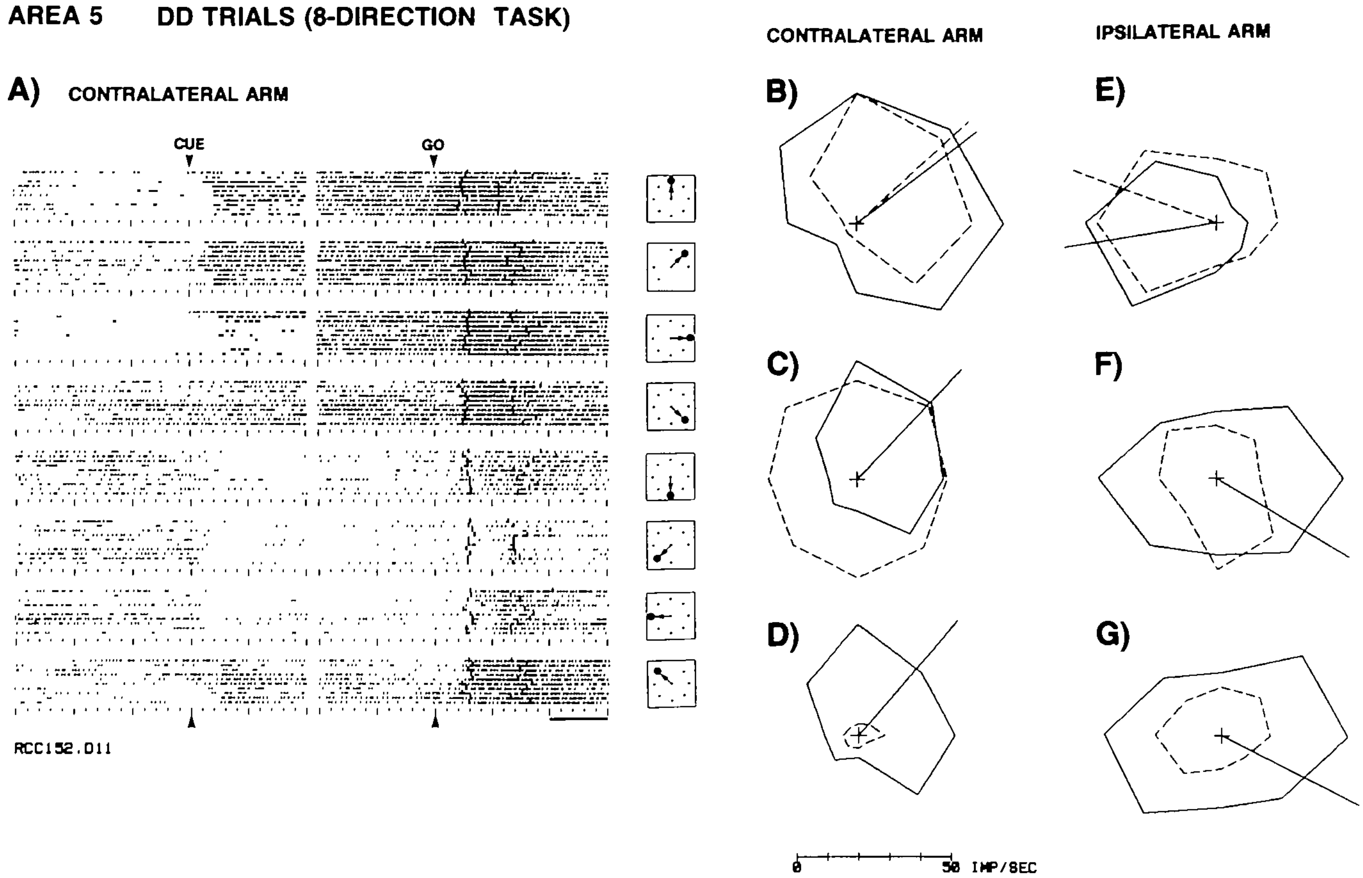

Figure 15. *A,* Raster representation of the responses of the cell in Figure 13 during instructed-delay trials of the eight-direction task, using the contralateral arm. The *target panel replicas* to the right of each raster indicate the cue location and movement direction. *B,* Polar-plot representation of the data from *A. Dashed polar plot,* discharge during the delay period. *Solid-line polar plot,* movement-related activity after the GO signal until the end of each trial. The two vectors are the preferred direction of the cell calculated during the corresponding epochs of the trial. *C,* Polar-plot representation of the same cell in the modified NOGO task of Figure 14*A. Solid-line vector* is the preferred direction of the post-GO activity. *D,* Polar-plot representation of the responses in Figure 14*B. E,* Responses of the same cell in the eight-direction task while using the ipsilateral arm. *F,* Responses of the same cell in the modified NOGO task of Figure 14*A* while using the ipsilateral arm. *G,* Responses of the same cell in the modified NOGO task of Figure 14*B* using the ipsilateral arm.

and 40, respectively, in premotor, 12 and 16 in parietal; $p > 0.05$, χ^2 test). However, there were also differences in the responses in the two areas. First, post-GO responses in premotor cortex were usually short-latency phasic increases or decreases in activity (Fig. 7*C,D*), whereas those in area 5 were predominantly tonic. Second, premotor cells responded to either the spatially matched (42 of 119 responses) or nonspatial GO signals (77 of 119 responses) or to both, but area 5 cells responded predominantly to the nonspatial signal (28 of 31 responses; $p < 0.01$, χ^2 test). Third, premotor cells could respond to nonspatial GO signals in both DD and NOGO trials (Figs. 6*B,D*; 7*B,D,F,H*), whereas area 5 cells responded only in NOGO trials. Fourth, about equal numbers of premotor cells showed post-GO responses in only one direction (25 of 52, Fig. 6*C,D*) or in both directions (27 of 52; Fig. 7*C,D*), whereas most area 5 cells (24 of 26) responded to pseudo-GO signals in only one direction ($p < 0.01$, χ^2 test). Fifth, the responses of relatively few premotor cells suggested the spatial interaction between competing target locations evident in area 5, and only one such cell (Fig. 7*E–H*) showed effects that approached the strength of the responses seen in Figures 9 and 13. Since premotor recordings were completed before the powerful effects were found in area 5 of monkey C, no premotor cells were studied in the NOGO task variants.

The differences in the responses of the two cortical areas to the pseudo-GO signals in NOGO trials is further circumstantial evidence that they are not simple passive sensory responses to the visual stimuli, but instead reflect differences in the task-related processing of the information provided by the visual cues.

Discussion

This study compared the contribution of dorsal premotor cortex and parietal area 5 to response selection using an instructed-delay task that included a GO/NOGO paradigm. The monkeys had to select the appropriate response according to four arbitrary associative rules with different levels of stimulus-response (SR) compatibility. In RT trials, they were not forewarned as to what to do prior to the GO signal. In DD and RD trials, a spatial cue signaled the direction of an impending movement either toward or away from the cue location. In NOGO trials, the location of the cue was irrelevant because it instructed the monkeys not to move. Trials were presented in a randomized-block sequence, and the monkeys could not anticipate which rule applied until the cue or GO appeared. A key assumption is that the instructed-delay trials require similar initial visuospatial analysis of the cues after their appearance, but that once their instructional content is discerned, they are distinguished from RT trials by the monkey's intention to move either toward or away from the cue, or not to move.

In both premotor cortex and parietal area 5, the initial cell responses to cues (<250 msec) tended to be similar in DD and NOGO trials. The two areas were distinguished by their subsequent delay-period behavior. The activity of many premotor cells in NOGO trials began to diverge from that in DD trials within 250 msec after cue presentation, and the mean population response at the end of the delay period was much less directional in NOGO trials than in DD trials. This effect, expressed primarily by a decrease in mean activity in NOGO trials in the preferred direction, is a presumed premotor correlate of the monkey's decision not to move to the target. In contrast, area 5 cells had a much stronger tendency to respond similarly throughout the delay period of DD and NOGO trials. The mean area 5 population signal covaried as strongly with the spatial location of the cues at the end of the delay period in NOGO as in DD trials, and did not reflect the monkeys' decision not to move to the same degree evident in premotor cortex.

Premotor Cortex and Response Selection

GO/NOGO tasks may be performed in two different ways, with important consequences for response selection (Petrides, 1986). Often, subjects are rewarded for responding to one stimulus and never rewarded after presentation of another. In this asymmetric paradigm, they acquire the NOGO response by extinction, learning to discriminate between the behaviorally relevant and irrelevant stimuli according to the differential reward schedule. In contrast, in a symmetric paradigm, subjects learn a conditional rule to select between two rewarded strategies, move or don't move, in response to two behaviorally relevant stimuli. Lesions of the periarcuate premotor cortex result in significant deficits in the performance of symmetric GO/NOGO tasks but not asymmetric tasks (Petrides, 1986). This indicates that the premotor cortex is critical for differential response selection using a learned conditional rule of specific SR associations (Mitz et al., 1991).

The present results also suggest that a large population of premotor cells contribute to the differential GO/NOGO response to directional signals in a distributed manner. The decision not to move in the present task was not paralleled by an absence of premotor activity changes. Instead, it involved responses in most task-related cells that often differed markedly from both the discharge correlated with the intention to move in DD trials and the preinstruction activity in RT trials. Although the nature of the NOGO response varied widely from cell to cell, the overall trend was for a suppression of activity at the preferred direction. We suggest that these complex single-cell responses are the premotor correlate of the distributed cognitive processes involved in selecting between the two rewarded motor strategies. This further supports the hypothesis that premotor cortex is implicated in response selection, not just in the preparation for the selected response (Mitz et al., 1991; di Pelligrino and Wise, 1993a,b). There was no new motor act to prepare in NOGO trials—the monkeys simply had to maintain the current arm posture. A previous study of premotor activity using a symmetric GO/NOGO task reported findings largely consistent with the present results (Wise et al., 1983; Weinrich et al., 1984).

Despite all the complicated single-cell responses in NOGO trials, the premotor population averages were very similar at the end of the delay period for the two cue locations, and much less directional than in DD trials (Fig. 4). The directionally tuned activity of cells in primary motor (Georgopoulos et al., 1988; Schwartz, 1993) and premotor cortex (Caminiti et al., 1991) has been interpreted as a signal that defines the spatial metrics of movements. There is no a priori reason to anticipate what might be the nature or the metrics of the decision not to move, but the relatively nondirectional premotor population responses might be a signal to maintain the arm at its current position.

Nevertheless, the majority of premotor cells were still directionally tuned at the end of the NOGO delay period, although less than in DD trials. Therefore, although the monkeys successfully selected the NOGO response, there was still evidence of an influence of the spatial locations of the cues on cell activity. This may reflect an underlying sensitivity of premotor cells to the direction of gaze or of attention (Boussaoud and Wise, 1993a,b) and to the spatial location of cues irrespective of their motor significance (di Pelligrino and Wise, 1993a,b).

SR compatibility provides a different perspective (Fitts and Seeger, 1953). SR compatibility relates to the naturalness or complexity of the mapping rules between stimuli and motor responses. This concept suggests that the CNS is organized in such a way that it has a propensity to emit certain motor responses to sensory stimuli. Reaching movements to the spatial location of stimuli are motor acts with high SR compatibility, whereas movements away from stimuli (RD trials) or not moving (NOGO trials) are responses of lower compatibility. The residual directional activity late in NOGO trials could represent the effect of lower SR compatibility on the selection of the same response to directionally different stimuli, or an incomplete suppression of the predisposition of the system to map spatial sensory inputs onto reaching movements directed toward the stimulus.

The other major feature of premotor activity was that the initial cue responses in DD and NOGO trials were similar. In the present task, trial types were randomized, and the spatial location of stimuli was relevant in defining the response metrics in RT, DD, and RD trials but not in NOGO trials. Nonspatial cues or blocks of similar trials may have produced different cell behavior. Alternatively, the initial response to the spatial signal could be "sensory," while later activity reflected more "motor" processes. However, even the earliest responses of premotor cells are modulated by the motor significance of cues, and are not "sensory" per se (Wise et al., 1983; Boussaoud and Wise, 1993a,b; di Pelligrino and Wise, 1993a,b). SR compatibility again provides a different explanation. According to this concept, selection of responses with the highest compatibility requires the least amount of neuronal processing and the shortest central delays. Responses with lower compatibility requiring more complex neuronal processing are expressed at longer delays. The similar initial cue responses in DD and NOGO trials result because the CNS rapidly selects the response with highest compatibility—reach toward the target. The decision not to move requires more complex neuronal events and is not expressed in premotor cell activity until after a further delay. In this view, even the earliest premotor cue responses could be considered "motor." This again supports a distributed representation of the GO/NOGO decision by different patterns of activity of a single population of cells.

A different model for the decision process predicts the selective activation of two separate cell populations that uniquely associate either the GO or the NOGO cue with the rewarded responses of moving or withholding movement, without regard to their metrics. Cell discharges recorded uniquely after cue or GO signals in NOGO trials have been reported in 11% of prefrontal (Watanabe, 1986; Sakagami and Niki, 1994), 19% of supplementary motor (Kurata and Tanji, 1985), and 22% of striatal neurons (Apicella et al., 1992). This was not observed in premotor cells (Wise et al., 1983; Weinrich et al., 1984; present results). This may reflect fundamental differences in the contribution of those structures to the performance of GO/NOGO tasks. The other structures may even be more crucial for the GO/NOGO decision, and then relay this information to premotor cortex, but lesion studies do not support this (Petrides, 1986).

Task design may have also contributed to the differences in results. The task used by Apicella et al. (1992) was closest to our own, but there was only a single reaching target and only a GO/NOGO choice. In the other studies, there was no true rewarded NOGO response and the cues did not define response metrics in any way. In the study by Kurata and Tanji (1985), monkeys always made a simple key-press movement, and the cue informed them only of the appropriate modality (auditory or vibrotactile) of the GO signal. The "NOGO" signals were only irrelevant stimuli of the inappropriate modality presented during the delay period between the cue and GO signals, which the monkeys had to ignore. In the prefrontal studies (Watanabe, 1986; Sakagami and Niki, 1994), the monkeys always made a key-release response to complex cues that had no spatial relationship to the response. GO trials required an immediate response after the GO signal (i.e., RT trials), whereas the "NOGO" trials only required that the movement be delayed for a brief self-paced time interval after the GO signal, making them equivalent to the delay period of our DD trials. We observed a number of premotor cells that were not very active after the GO signals of RT trials but were strongly directionally active after the cue signals of DD trials (Crammond and Kalaska, unpublished observations). In the terminology used in the prefrontal studies, these would be "NOGO-specific" cells. A final factor may be search bias. We screened for cells that were active in the eight-direction task and then selected some of those for further study in the response-selection task. The possibility remains that a larger population of premotor cells than that found in this study are preferentially active in NOGO trials.

Representation of a Possible Visuomotor Mapping Function in Parietal Area 5

Area 5 cell responses in the GO/NOGO task do not appear consistent with a simple interpretation of either of the traditional higher-order somatosensory or motor roles for area 5.

The activity changes during an instructed-delay period refute the simple hypothesis that area 5 generates an unambiguous neuronal representation of current body posture and movement under all conditions (Kalaska et al., 1990), since they could be misconstrued as a shift in arm posture even though it had not changed. Alternatively, the activity changes in DD trials could be a centrally generated corollary signal about the intended movement that would be used to interpret the reafferent input from the limb as the movement unfolds (Kalaska, 1988, 1991; Matthews, 1988). However, this does not explain the activity in NOGO trials, when the monkey does not intend to move and no movement-related reafferent signals will arise.

Delay period activity in area 5 covaries with intended movement direction in DD trials (Crammond and Kalaska, 1989, unpublished observations; Ferriana and Bianchi, 1994) and so could contribute to response selection and movement planning (Seal et al., 1982, 1983). However, the continued discharge in NOGO trials does not fit readily into this role either. This would require that area 5 contributes to response selection only when the monkey intends to make an overt movement (DD trials), but not to the specific decision not to move (NOGO trials). Admittedly, nearly half of the area 5 cells showed modest but significantly different responses near the end of the delay period of DD and NOGO trials (Table 1). In the strictest sense, therefore, the activation state of the parietal sample was discriminably different between GO and NOGO trials, from which one could argue that area 5 can contribute to the GO/NOGO decision. However, any such contribution by area 5 would be much more subtle than that in premotor cortex.

The sustained delay period activity and the responses to GO signals in NOGO trials were probably not passive visual responses in the usual sense. The part of area 5 located medial and deep in the intraparietal sulcus, called MIP, may have a "visual" component to its activity (Colby et al., 1988; Colby and Duhamel, 1991; Savaki et al., 1993). We cannot prove that the cells in monkey C with the strongest modulation by GO signals in NOGO trials were in fact in MIP (Figs. 2, 3), but our results reveal the degree to which any such putative visual component in area 5 is modulated by behavioral context. For instance, cell activity in the post-GO period of catch DD trials was not strongly modulated by the appearance of all targets, and failed to signal their presence as the monkeys moved an arm toward one of them. In contrast, cell activity was sustained after extinction of the cues in MEM trials, and so signaled their motor instructional significance and not their disappearance. Furthermore, the behavior of the cell tested with both arms showed clearly that at least for that particular neuron, the strong responses evoked by the cues were not just a passive response to the spatial location of stimuli, but were more closely related to how the monkey intended to respond to them (DD trials) or would respond to them if permitted (NOGO trials). Finally, the late delay period activity of area 5 cells in RD trials covaries mainly with intended movement direction and not with cue location (Kalaska and Crammond, 1990, unpublished observations). The same behavior is seen in premotor cells (Crammond and Kalaska, 1994) but not in many prefrontal cells during a similar "antisaccade" task (Funahashi et al., 1990).

A working hypothesis to account for these response properties is that at least part of area 5 is implicated in the processing of somatic and visually derived information about the relative spatial locations of body parts and external stimuli for the guidance of limb movements (Stein, 1989; Goodale and Milner, 1992; Colby et al., 1993). The cells are recipient not to simple visual inputs, but to a centrally generated representation of target-related information in motor coordinates at a stage in the control process antecedent to the decision of whether or not to act. This representation likely covaries with the kinematics of movement, whereas precentral cortex activity is more strongly modulated by movement kinetics (Kalaska et al., 1990). The response of the cell in Figure 15 suggests that this signal is in arm-centered coordinates (Caminiti et al., 1991; Flanders et al., 1992; Ferraina and Bianchi, 1994), but results are too preliminary to draw a strong conclusion. Likewise, it is not yet possible to decide whether the discharge signals extrinsic kinematic attributes such as the spatial location of the potential movement target relative to the arm, or could represent intrinsic kinematic attributes of the arm movement the monkeys would make to it, such as joint motions or changes in arm postures. The results also indicate that parallel representations of potential motor responses to external stimuli and of the actual intended motor response to them can coexist in area 5 and premotor cortex, respectively.

This visuomotor mapping function is reminiscent of the behavior predicted for neuronal elements in the visual-proprioceptive association maps of several "progressive matching" or associative learning models for the sensorimotor transformations underlying reaching movements (Jeannerod, 1991; Mel, 1991; Burnod et al., 1992; Bullock et al., 1993). According to these models, visual and proprioceptive signals converge onto a cell population whose role is to learn the mapping between current arm postures and target spatial locations. Selective activation of cells with specific combinations of preferred arm posture and visual stimulus locations define the required reach trajectory. However, these models generally predict that the cells should be unconditionally driven by specific combinations of arm posture (or movement) and stimulus location, irrespective of the motor response of the animal. This would account for the NOGO trial responses of area 5 cells, but the activity in MEM and RD trials, and their post-GO behavior in DD trials show that cell activity is not unconditionally dependent on visual stimulus presence. Moreover, the task responses of many area 5 cells could not be explained by the simple summation of convergent passive somatic and visual inputs. Instead, they became evident only when the monkey was performing the task or otherwise interacting with the immediate environment.

Notes

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