Reaching Movements With Similar Hand Paths but Different Arm Orientations. II. Activity of Individual Cells in Dorsal Premotor Cortex and Parietal Area 5

STEPHEN H. SCOTT, LAUREN E. SERGIO, AND JOHN F. KALASKA
Centre de Recherche en Sciences Neurologiques, Université de Montréal, Montreal, Quebec H3C 3J7, Canada

Scott, Stephen H., Lauren E. Sergio, and John F. Kalaska. Reaching movements with similar hand paths but different arm orientations. II. Activity of individual cells in dorsal premotor cortex and parietal area 5. *J. Neurophysiol.* 78: 2413–2426, 1997. Neuronal activity in primary motor cortex (MI) is altered when monkeys make reaching movements along similar handpaths at shoulder level with two different arm orientations, either in the natural orientation with the elbow positioned below the level of the shoulder and hand or in an abducted orientation with the elbow abducted nearly to shoulder level. The present study examines to what degree two other cortical areas, the dorsal premotor (PMd) and parietal area 5, also show modulation of cell activity related to arm geometry during reaching. The activity of most (89%) of the 207 cells in PMd recorded while monkeys made reaching movements showed a statistically significant change in activity between orientations [analysis of variation (ANOVA), $P < 0.01$]. A common effect of arm orientation on cell activity was a change in the overall level of discharge either before, during, and/or after movement (67%, ANOVA, task main effect, $P < 0.01$). Many cells (76%) showed a statistical change in their response to movement direction (ANOVA, task × direction interaction term, $P < 0.01$), including changes in dynamic range and changes in the preferred direction of cells that were directionally tuned in both arm orientations. Overall, these effects were similar qualitatively but not as strong quantitatively as those observed in MI. A sample of cells was recorded in area 5 of one monkey. Most (95%) of the 79 area 5 cells showed a change in activity when reaching movements were performed using different arm orientations (ANOVA, $P < 0.01$). As in PMd and MI, many area 5 cells (56, 71%) showed changes in their tonic discharge before, during, and/or after movement, and 70 cells (89%) showed changes in their response to movement direction (ANOVA, task × direction interaction term, $P < 0.01$). The observed changes in neuronal activity related to posture and movement in MI, PMd and area 5 demonstrate that single-cell activity in these cortical areas is not simply related to the spatial attributes of hand trajectory but is also strongly influenced by attributes of movement related to arm geometry.

INTRODUCTION

Reaching to a visual target in space is assumed widely to require a series of sensorimotor transformations to convert a signal about target location on the retina into a pattern of peripheral motor output signals to muscles to move the hand to the target. A major focus of neurophysiological studies of reaching movements has been to identify the types of information and neuronal processes that each brain region contributes to this sensorimotor task (Georgopoulos 1991; Kalaska 1991a, 1995; Kalaska and Crammond 1992; Soechting and Flanders 1992).

The nature of the movement-related information conveyed in a brain region commonly is inferred by the correlation between the discharge of its individual cells with different variables of movement. Two important classes of variables include those related to the global goal of the task, such as target location and hand position or movement, and those related to the causal mechanical details of the arm movement, such as joint angle changes, joint torques, and electromyographic patterns. This latter class will be referred to as intrinsic variables whereas the former will be referred to as extrinsic to distinguish between variables that explicitly specify or depend on the geometry of the limb (intrinsic) from those that do not (extrinsic). In regions such as primary motor cortex (MI), neuronal discharge has been correlated to both classes of variables (Cheney and Fetz 1980; Crutcher and Alexander 1990; Evarts 1968; Fu et al. 1995; Georgopoulos et al. 1982, 1988; Humphrey 1972; Scott 1997; Shen and Alexander 1997a; Zhang et al. 1997). While this may reflect the parallel and distributed nature of neuronal processing, it also may reflect the fact that extrinsic and intrinsic movement variables are coupled highly and so often are confounded in task design and data analysis (Lacquaniti et al. 1995; Mussa-Ivaldi 1988). Further progress on the nature of the information processed in a given cell and cortical region must dissociate these different movement variables (Caminiti et al. 1990, 1991; Crutcher and Alexander 1990; Kalaska et al. 1989; Scott and Kalaska 1997; Shen and Alexander 1997a,b; Zhang et al. 1997).

Toward this goal, a previous study analyzed the activity of cells in MI of monkeys while they performed reaching movements to targets using similar hand trajectories but different arm orientations (Scott and Kalaska 1997). This paradigm provided a separation between intrinsic variables related to the peripheral motor apparatus, which varied substantially between arm orientations, from extrinsic variables that remained relatively constant. Most cells in MI showed a significant change in their level of discharge or in their directional tuning, or both, between arm orientations before, during, and/or after movement when the monkey maintained a constant arm posture at the peripheral targets. The observed changes in cell discharge do not necessarily mean that the neural representation of movement and posture in MI changed between the two arm orientations. On the contrary, modeling studies (Scott and Kalaska 1997) demonstrated that cells with a fixed relationship to specific peripheral motor parameters would undergo the same types

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of alterations in discharge between arm orientations as shown by the MI cells. In these models, changes in cell activity occurred because the specific mapping between the direction of hand movement within the fixed plane of the task and the parameter space for each cell changed as a function of arm orientation.

An interesting question is whether cells in dorsal premotor (PMd) show the same sensitivity to arm geometry. PMd has been more implicated in higher order processes of response selection and movement planning than MI (di Pellegrino and Wise 1991, 1993; Kurata 1993; Mitz et al. 1991; Okano and Tanji 1987; Shen and Alexander 1997b; Weinrich and Wise 1982; Wise et al. 1996). Psychophysical studies have suggested that these higher-order planning processes may be concerned mainly with extrinsic variables describing the spatiotemporal motion of the hand rather than with intrinsic variables of the task (Flash 1987; Gordon et al. 1994; Morasso 1981). This leads to the prediction that PMd cells may be less sensitive to arm orientation than cells in MI. Caminiti et al. (1991) found that when monkeys made reaching movements in different parts of space, the directional tuning of PMd cells tended to rotate systematically with the starting shoulder angle in a manner similar to cells in MI. However, the directional tuning of cells related to movement in different body-, head-, or eye-centered coordinate frames all may rotate systematically when the task is performed in different parts of space. Therefore, the similar degree of rotation of the preferred direction of cells in PMd and MI may have had different origins, such as different degrees of sensitivity to intrinsic versus body-centered extrinsic variables. It appeared worthwhile to reexamine this question by recording from PMd cells in the same animals used to study MI activity during movements with similar hand trajectories but different arm orientations.

Parietal area 5 also has been implicated in the distributed limb control system (Ashe and Georgopoulos 1994; Ferraina and Bianchi 1994; Kalaska 1991b, 1996; Kalaska and Crammond 1992; Kalaska et al. 1983). The second purpose of the present study was to clarify further the nature of the representation in area 5 (extrinsic vs. intrinsic) by examining whether cell discharge in this region was altered when reaching movements were made using similar hand trajectories but different arm orientations.

METHODS

Task apparatus and design

The experimental paradigm and task apparatus have been described in detail elsewhere (Kalaska et al. 1989; Scott and Kalaska 1997). Briefly, two juvenile male rhesus monkeys (*Macaca mulatta,* 4–6 kg) were trained to make visually guided reaching movements from a central position to eight peripheral LED targets. The eight target lights were presented five times in a randomized-block design.

The monkeys performed the task using two different arm orientations (Scott and Kalaska 1997). In the first orientation, the monkey grasped the handle at about shoulder height and moved the manipulandum using its preferred, natural arm orientation with the elbow below a line joining the hand and shoulder. In the abducted orientation, a clear Plexiglas barrier was positioned immediately below the handle, so that the monkey had to abduct its arm to grasp the handle and move the manipulandum. The magnitude of abduction was ~80° so that the hand, elbow, and shoulder formed a near-horizontal plane that varied slightly with the position of the manipulandum (see Scott and Kalaska 1997).

After training, standard aseptic surgical techniques were used to prepare the monkeys for recording in the precentral gyrus or in parietal area 5 (Kalaska et al. 1989, 1990).

Data collection

Standard recording methods were used to study the activity of individual cells in PMd and area 5 on the side contralateral to the arm used to make reaching movements (Kalaska et al. 1989). During each recording session, a microelectrode was advanced through the cortex while the monkey performed arm movements either in the natural or abducted arm orientations. Cells related to the motor task were isolated and tested in the task. The activity of each cell was recorded while the monkey performed five complete replications of eight movements first in one orientation and then in the other. No specific order was followed so that there were approximately equal numbers of cells recorded initially in each orientation.

Near the end of the experiment, electrolytic lesions (25 μA, 10 s) were made at several locations within each recording chamber to confirm the location of penetrations in both cortical regions. At the end of an experiment, monkeys were anesthetized deeply with barbiturates and perfused with buffered saline followed by formalin. Pins were inserted at known grid-map coordinates to identify the region where cell recordings were made. The precentral and parietal cortices were sectioned and stained to permit localization of the marked penetrations.

Throughout all stages of the experiment, the guidelines and principles respecting the use of animals in research, approved by the Canadian Council on Animal Care, were followed.

Data analysis

The analysis of cell discharge variation with movement direction and arm orientation has been described elsewhere (Kalaska et al. 1989; Scott and Kalaska 1997). Briefly, each trial was divided into three behavioral epochs: center hold time (CHT) when the monkey remained at the central target prior to the illumination of the target LED; a combined reaction and movement time (RT + MT) from the illumination of the target light to the end of the arm movement; and target hold time (THT) from the end of the movement to the end of the trial (Kalaska et al. 1989). Direction was defined by trigonometric convention with 0° pointing to the right and angle increasing counterclockwise. Data collected when the monkey performed the task with the left arm were mirror-image transposed whenever cell responses from both arms were pooled.

A nonparametric ''bootstrapping'' test was used to identify whether a cell was directionally tuned (Crammond and Kalaska 1996; Georgopoulos et al. 1988; Scott and Kalaska 1997). Briefly, the directional bias of a cell was characterized by a mean vector, the orientation of which defines the cell's preferred movement direction (Batschelet 1981; Georgopoulos et al. 1982). The length of the mean vector was defined from a given cell's discharge across all movement directions, as recorded in the task, and compared with the mean vector obtained from a shuffling procedure that randomly reassigned single-trial data to different ''movement directions.'' The cell was considered directionally tuned if the length of no more than 40 of 4,000 shuffled mean vectors exceeded the task-related mean-vector length of the cell ($P < 0.01$).

Variations in cell discharge with movement direction and/or arm orientation were evaluated using several tests. A split-plot analysis of variance (ANOVA) was used to evaluate whether changes in the overall level of cell discharge or its relationship to movement direction was significantly modulated by arm orientation

($P < 0.01$) (Snedecor and Cochran 1980). Two experimental effects were determined with this unbalanced ANOVA: a main effect between task conditions reflecting a change in the overall level of cell discharge between the two arm orientations and a task × direction interaction signifying a change in the nature of the relationship of cell discharge with movement direction. This interaction could take at least two forms: a task × direction interaction effect could reflect a change in the dynamic range of the cell's directional tuning curve, defined as the difference between the maximum and minimum discharge level across the 8 movement directions. At the extreme, a cell could be tuned directionally in one arm orientation but nondirectional in the other (dynamic range of 0). To test for the presence of this type of interaction, the dynamic range of the cell was defined for each of the five replication tuning curves for each arm orientation. A *t*-test was applied to test for a significant difference between the five replication dynamic ranges recorded in each arm orientation.

The task × direction interaction effect also may reflect a change in the directional preference of the cell between arm orientations. Cells unimodally tuned to the direction of movement in both arm orientations were analyzed further to evaluate whether there was a change in their preferred direction between arm orientations. The preferred direction of a cell was calculated separately for each of the five replicated blocks of movements to each of the eight target locations providing five replicated estimates of a cell's preferred direction for each arm orientation. The Watson-Williams test (Batschelet 1981) identified whether there was a statistical change ($P < 0.01$) in the mean angle of the two distributions of five replication preferred directions for each arm orientation (see Scott and Kalaska 1997). This tests only differences between the preferred direction of a cell for each arm orientation based on the variance of the preferred direction signal in repeated blocks of trials and not on the total directional variance of the pattern of cell activity as expressed in the tuning curve (Scott and Kalaska 1997).

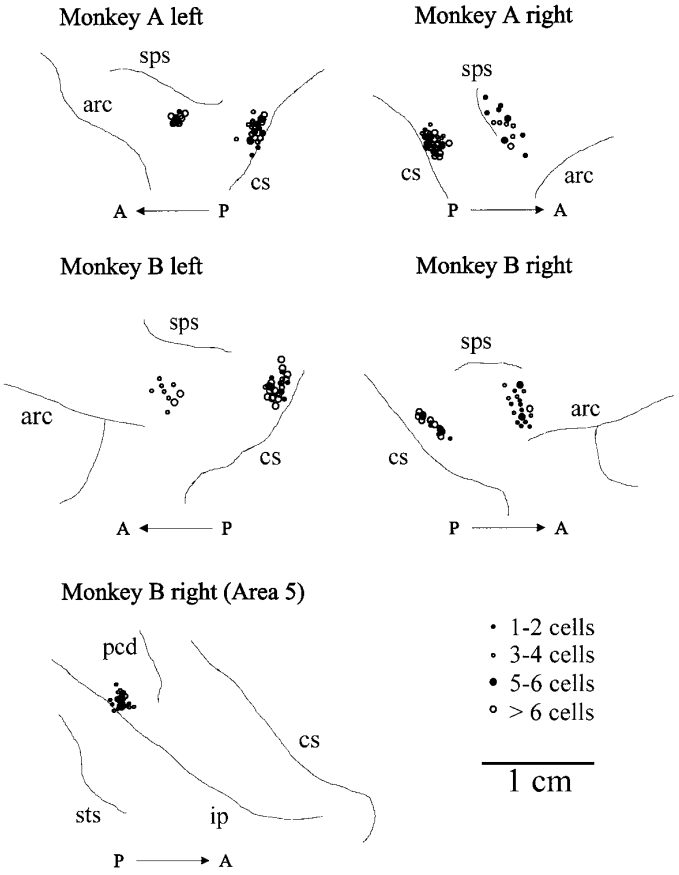

FIG. 1. Distributions of the recording sites of cells in the precentral and postcentral gyrii of 2 monkeys. Rostral and caudal clusters of penetrations in the *top 4* diagrams indicate the recording sites for dorsal premotor (PMd) and primary motor (MI) cortex, respectively. Recording sites rostral to the intraparietal sulcus (*bottom*) indicate the locations of penetrations for parietal area 5 cortex. cs, central sulcus; sps, superior precentral sulcus; arc, arcuate sulcus; ip, intraparietal sulcus; pcd, postcentral dimple; sts, superior temporal sulcus; A, anterior; P, posterior.

RESULTS

Cell database

The activity of 207 cells was recorded in the anterior precentral gyrus in four hemispheres of two rhesus monkeys that also were used for a study of MI discharge in the same task (Scott and Kalaska 1997). For the first monkey, 67 and 49 cells were recorded in the left and right hemispheres, respectively, and for the second monkey, 38 and 53 cells were recorded in the left and right hemispheres, respectively (Fig. 1). The cells recorded in the anterior clusters of penetrations in each hemisphere (Fig. 1, *A–D*) were considered to be in premotor cortex because microstimulation (11 pulses, 0.2-ms duration, 330 Hz) at these sites failed to evoke visible movement of the limb or contractions of any muscles at stimulus strengths ≤50 μA, a physiological criterion frequently used to demarcate dorsal premotor cortex from primary motor cortex (Crammond and Kalaska 1996; Kurata 1989; Kurata and Tanji 1986; Tanné et al. 1995; Weinrich and Wise 1982). Examination of histological sections confirmed that the anterior clusters of penetrations in Fig. 1 were all made in a region of cortex in which large lamina V pyramidal cells (>29 μm) were rare or absent (i.e., cytoarchitectonic area 6). The cells recorded in the posterior cluster of penetrations in each hemisphere (Fig. 1, *A–D*) were in the anterior bank of the central sulcus (primary motor cortex) and were described in a previous article (Scott and Kalaska 1997). The activity of 79 cells was recorded in parietal area 5 cortex in the right hemisphere of the second monkey. Cell recordings were confined to the most superficial 2–3 mm of the anterior (or medial) bank of the intraparietal sulcus (Fig. 1). No cell data were collected from the part of area 5 located deep in the intraparietal sulcus.

Cells included in this study were directionally tuned in at least one of the behavioral epochs (RT + MT or THT) in one of the two arm orientations and frequently for both epochs and orientations. As shown previously (Caminiti et al. 1991; Kalaska et al. 1983), cell activity in PMd and area 5 varied continuously with the direction of hand movement centered on a preferred direction of movement. The response properties of cells in PMd recorded in each hemisphere were similar and the results will be described for the entire sample of cells pooled from all hemispheres.

Arm orientation had a significant effect on the discharge patterns of most cells in PMd (89%) and area 5 (95%) during reaching movements (F test, $P < 0.01$, Table 1). Figure 2 highlights the pronounced change in activity for one cell in PMd and one in area 5. In the natural arm orientation, the PMd cell shows a strong phasic burst for a broad range of movements to the right and away from the monkey,

TABLE 1. *Variation of PMd, A5, and MI cell activity with arm orientation during reaching*

	PMd	Area 5	MI*
n	207	79	619
Level of activity (task main effect)			
CHT	74 (36)	28 (35)	354 (57)
RT + MT	87 (42)	40 (51)	326 (53)
THT	78 (38)	39 (50)	317 (51)
Any epoch	139 (67)	56 (71)	500 (81)
Movement direction (task X direction interaction)			
RT + MT	122 (59)	49 (62)	458 (74)
THT	113 (55)	60 (76)	506 (82)
Any epoch	158 (76)	70 (89)	568 (92)
Tonic activity or movement direction			
RT + MT	148 (72)	60 (76)	513 (83)
THT	138 (67)	63 (80)	547 (88)
Any epoch	184 (89)	75 (95)	593 (96)

F test, $P < 0.01$. Values in parentheses are percentages. *n*, number of cells. PMd, dorsal premotor cortex; MI, primary motor cortex; CHT, center hold time; RT + MT, combined reaction time and movement time; THT, target hold time. * Data for MI from Scott and Kalaska (1997).

with a preferred direction at 35° for RT + MT epoch. In the abducted orientation, the cell is tuned more narrowly and phasic for movements only to the right (preferred direction is 348°) and the magnitude of the burst is diminished greatly. The activity of the area 5 cell is altered strongly by arm orientation such that it is tuned strongly for movements away from the monkey at 71° in the abducted orientation but is almost silent for the same movements in the natural orientation and only weakly tuned at 287°. Note also the increase in tonic activity during CHT in the abducted orientation.

Variation of cell activity with arm orientation in PMd

CHANGES IN DISCHARGE LEVEL. As seen previously in MI, a common effect of arm orientation was a change in the overall level of cell activity in PMd (Fig. 3*A*). The average level of cell discharge between orientations was compared for each of the three behavioral epochs (Table 1). In PMd, tonic discharge during CHT changed between natural and abducted conditions in 74 (36%) cells. Average absolute change in tonic activity during CHT between natural and abducted arm orientations was 3.9 spikes/s. However, the distribution of change in tonic activity was distributed randomly about zero (Fig. 3*A*) such that the average level of discharge of cells in the two arm orientations was similar (10.4 and 11.3 spikes/s for natural and abducted orientations; paired *t*-test, $P > 0.10$). Similar percentages of cells showed changes in the grand mean of activity measured across all eight directions during RT + MT (42%) and THT (38%) between the two orientations (Table 1). As well, changes in cell activity between arm orientations tended to be coupled for the three behavioral epochs (Fig. 4, *A–C*). Cells that showed a large change in cell discharge between arm orientations in one behavioral epoch tended to show a large change in discharge of the same sign (increase or decrease) for the other behavioral epochs (CHT vs. RT + MT, $r = 0.69$; CHT vs. THT, $r = 0.67$ and RT + MT vs. THT, $r = 0.83$; $P < 0.01$ for all).

This influence of arm orientation on the overall level of activity was more modest in PMd than in MI (Scott and Kalaska 1997). For instance, the proportion of cells showing a significant difference in the level of activity between arm orientations was significantly lower in PMd than in MI in all three epochs (CHT, RT + MT, THT; Table 1, $P < 0.01$, χ^2 test). The absolute mean change in tonic activity during CHT was also less in PMd than in MI (mean change 7.2 spikes/s for MI; *t*-test, $P < 0.001$). Figure 5*A* shows the cumulative distributions for the absolute change in firing rate observed for cells during CHT in each of the different cortical regions. In Fig. 5*A*, the greater the change in tonic activity for a given population of cells between orientations, the more the cumulative distribution curve deviates away from the ordinate (*Y*) axis. The cumulative distribution for PMd was closer to the ordinate axis than the cumulative distribution for the population of cells recorded from MI (Wilcoxon-Mann-Whitney test, $P < 0.001$). This reduced sensitivity of the activity level of PMd cells to changes in arm orientation partially may reflect the fact that their average tonic level of discharge was lower than observed in MI (13.7 and 14.2 spikes/s for natural and abducted orientations). However, when cell discharge changes for a given cortical region were normalized to its average level of tonic discharge, MI cells still tended to show larger changes in discharge between arm orientations (Wilcoxon-Mann-Whitney test, $P < 0.01$; normalized curves not shown).

CHANGES IN DIRECTIONAL TUNING. The majority of PMd cells (76%) demonstrated a task × direction interaction effect during either RT + MT or THT or both (*F* test, $P < 0.01$, Table 1). This interaction effect signifies a change in the relationship between cell discharge and movement direction between arm orientations that often reflected a modulation in the sharpness of cell tuning for reaching movements using different arm orientations or a change in the directional preference of the cell and often both. At the extreme, cells could be directionally tuned in one arm orientation but not in the other. For RT + MT, a majority of cells in PMd (160/207, 77%) were directionally tuned in both arm orientations, but 21 and 18 cells in the present sample were identified as unimodally tuned only in the natural or abducted orientations, respectively, but not in both (bootstrap test for directionality, $P < 0.01$). Eight cells were not directionally tuned in either orientation during RT + MT epoch. Of the 160 cells directionally tuned in both orientations, 92 (58%) showed a significant task × direction interaction. Forty-two (46%) of the 92 cells with significant interaction effects also showed a significant difference in the dynamic range of the five replicated tuning curves between the two arm orientations (*t*-test, $P < 0.01$), indicating that a change in the depth of modulation of their directional tuning curve contributed to the task × direction interaction.

A second factor that contributed to a statistical difference in a cell's response to movement direction between arm orientations was a change in its preferred direction of movement. Figure 3*B* illustrates that cells that did not show a significant task × direction interaction effect tended to show only modest changes in directional tuning as compared with

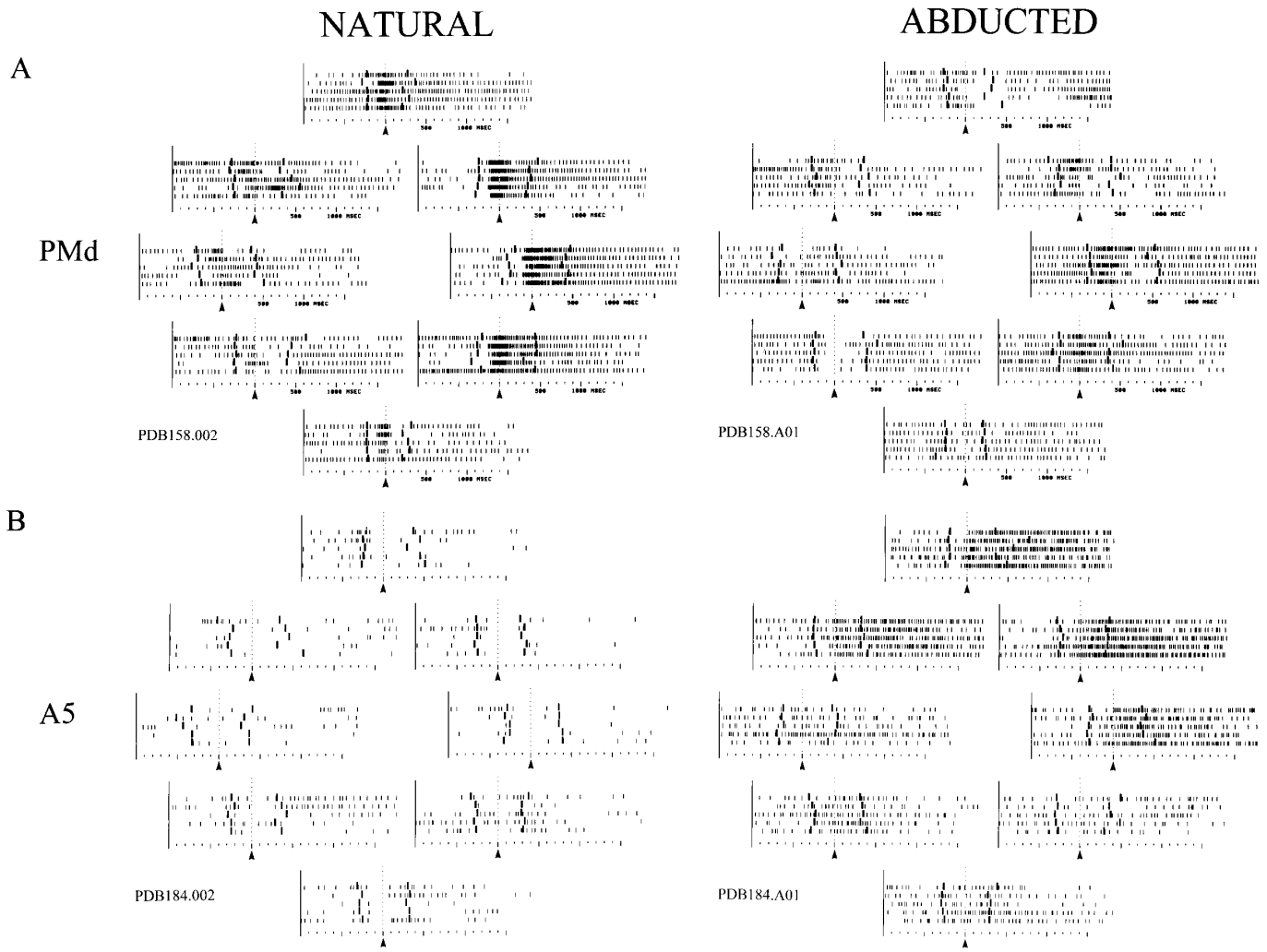

FIG. 2. *A*: response of a PMd cell during reaching movements in the natural (*left*) and abducted (*right*) arm orientations. Each raster illustrates the discharge pattern of the cell during 5 repeated trials to each target. Arrowhead, start of movement; thicker bars (*left* and *right* of arrowhead on each raster line) denote the onset time of the target light and the end of movement, respectively. *B*: response of an area 5 (A5) cell during reaching movement in the 2 arm orientations.

cells showing significant interactions. This is confirmed in Fig. 6*A* by the significant difference (nonparametric test for dispersion, $P < 0.01$) (Batschelet 1981) in the cumulative distribution of changes in directional tuning between cells with and without significant interaction effects. Cells directionally tuned in both arm orientations for a given epoch were analyzed further to determine whether their preferred directions of movement changed (directional shift) between arm orientations. For RT + MT, the directional preference of 40/158 (25%) of these PMd cells were significantly different between the two orientations (Watson-Williams test, $P < 0.01$, 2 cells could not be analyzed for this test). There was a broad continuum in the change in directional tuning of cells; although many cells showed only a small directional shift between orientations, the directionality of some cells was altered dramatically by arm orientation (Fig. 3*B*). The average absolute shift in directional tuning between orientations for RT + MT was 23.3°, whereas the average change in directional tuning (arithmetic mean) across all cells was only 6.0° clockwise.

Changes in the directional tuning of cells between arm orientations tended to be slightly larger during the THT epoch. The number of cells directionally tuned in both arm orientations dropped to 137 (66%), whereas the number directionally tuned in only the natural or abducted orientations increased to 27 and 30 cells, respectively. Of the 137 cells directionally tuned in both arm orientations, 73 (53%) showed a significant task × direction interaction, and 29 of these 73 cells (40%) with a significant interaction also showed a significant difference in their dynamic range of the five replicated tuning curves between arm orientations (*t*-test, $P < 0.01$). Of those cells directionally tuned in both arm orientations, 50 (37%) showed a statistical change in their preferred direction between orientations (Watson-Williams test, $P < 0.01$). The average absolute change in directional tuning was 36.0°, which was larger than observed during RT + MT epoch (nonparametric test for dispersion, $P < 0.02$). The arithmetic mean change in directional tuning during THT was 10.2° clockwise.

The directionality of PMd cells was generally less sensitive to changes in arm orientation than cells in MI during RT + MT epoch. For instance, the proportion of cells that

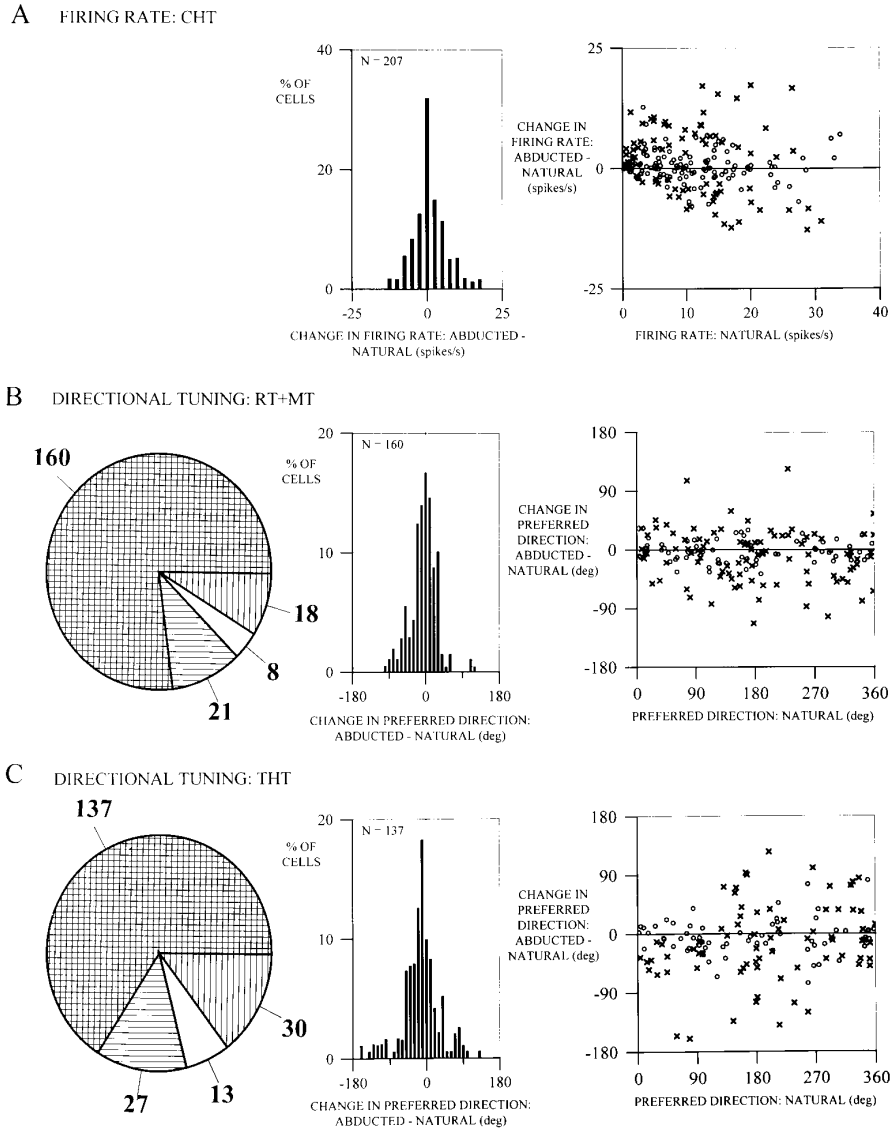

FIG. 3. Changes in the activity of PMd cells during reaching movements in different arm orientations. *A*: frequency histogram (*left*) of difference in the level of tonic discharge of cells during center hold time (CHT) between abducted and natural orientations (bin size 2.5 spikes/s, central bin ± 1.25 spikes/s). Scatter plot (*right*) shows the relationship between the level of discharge of each cell during CHT in the natural arm orientation vs. the magnitude of change in discharge between orientations. ×, cells with a significant difference in discharge ($P < 0.01$, F test); ○, cells with no significant difference ($P > 0.01$). *B* and *C*: pie-charts (*left*) show the proportion of cells directionally tuned in the natural orientation only (horizontal lines), abducted orientation only (vertical lines), and in both (hatched), as well as those not directionally tuned in either arm orientation (unfilled). Number of cells in each group is indicated beside each pie slice. Frequency histograms (*middle*) illustrate the change in directional tuning of cells between natural and abducted orientations (bin size 10°, central bin ±5°, positive value denotes a counterclockwise rotation in preferred direction from natural to abducted orientations). Scatter plots (*right*) show the relationship between the preferred direction of movement of each cell in the natural orientation vs. the magnitude of change in the preferred direction between orientations. Symbols denote statistical significance (F test, $P < 0.01$) as in scatter plot of *A*.

showed a significant difference in activity with movement direction (F test, task × direction interaction, Table 1) was smaller in PMd than in MI ($P < 0.01$, χ^2 test). Of the cells that were tuned in at least one orientation (bootstrap test for directionality), 39/199 PMd cells (20%) were directionally tuned in only one orientation, whereas 168/590 MI cells (28%) were directionally tuned in only one orientation ($P < 0.05$, χ^2 test). For cells that were directionally tuned in both arm orientations, the proportion of cells that showed a significant change in preferred direction (Watson-Williams test, Table 1) was lower in PMd (40/158; 25%) than in MI (203/422; 48%; $P < 0.01$, χ^2 test). Further, the average directional shift for PMd cells was smaller than for MI cells (Fig. 5*B*, 23.3 vs. 45.6°, nonparametric test for dispersion, $P < 0.01$) (Batschelet 1981).

In contrast, the effect of arm orientation on the directionality of PMd and MI cells was more similar during THT epoch. The average directional shift for PMd cells increased significantly from 23.3° in RT + MT to 36.0° in THT epoch (nonparametric test for dispersion, $P < 0.01$). In contrast, the average directional shift for MI cells decreased significantly from 45.6 to 39.0° between RT + MT and THT ($P < 0.01$) so that there was no difference in the average absolute directional shift for MI and PMd cells during THT ($P > 0.05$, Fig. 5*C*). Of the cells directionally tuned in at least one orientation during THT, a greater proportion of cells in PMd (57/194, 29.3%) compared with MI (109/604, 18.0%) were directionally tuned in only one orientation ($P < 0.05$, χ^2 test). However, the proportion of cells that showed a statistical change in activity with target location during THT (F test, task × direction interaction, Table 1) was smaller in PMd than in MI ($P < 0.01$, χ^2 test).

There was no observed correlation between changes in directional tuning for movement and posture in PMd cells. For cells directionally tuned in both epochs, the correlation in the magnitude and sign of the directional shift between RT + MT and THT was nearly zero ($r = 0.06$, $P > 0.05$). Therefore, cells in PMd with a large change in directional tuning during movement did not necessarily continue to show large changes in directionality related to maintaining constant arm postures at the peripheral targets using different arm orientations. This contrasts with the observed coupling

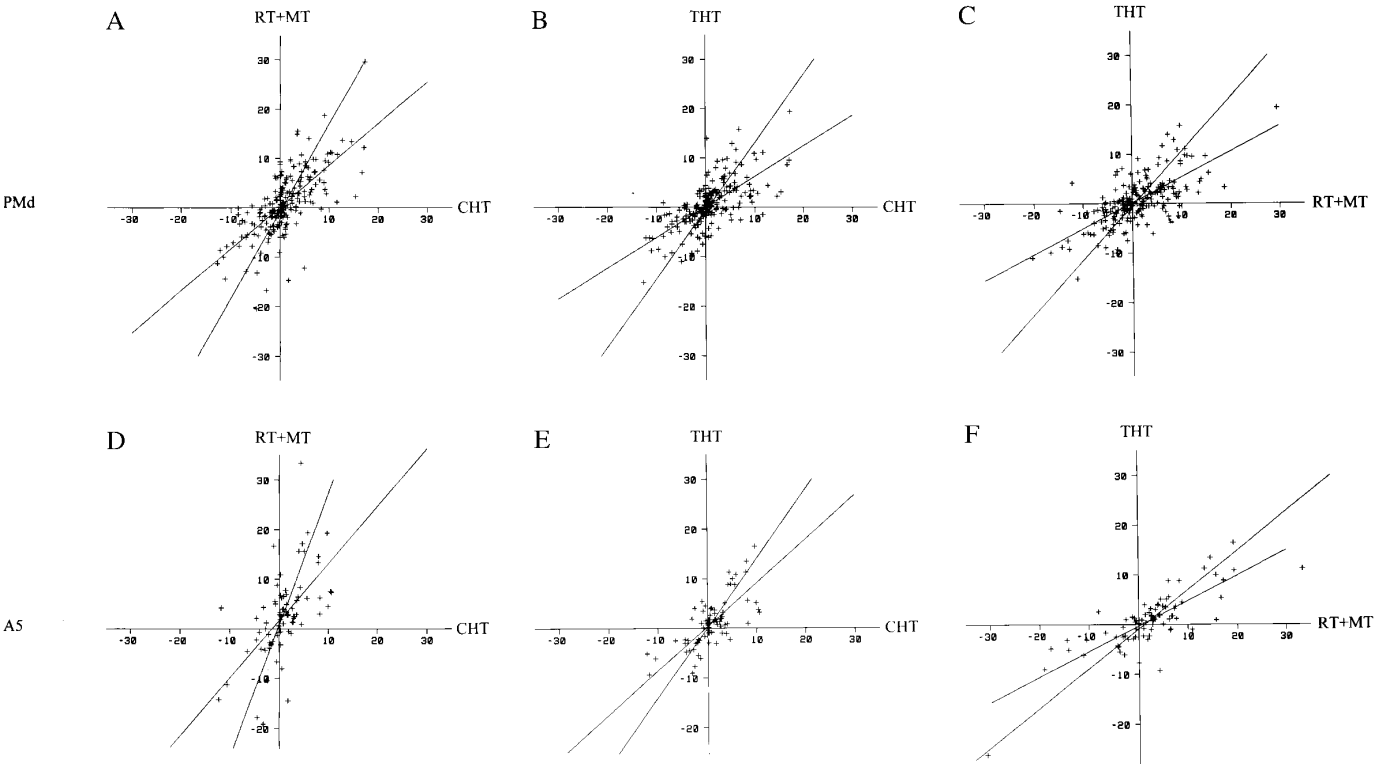

FIG. 4. Comparison of the change in the overall level of discharge between arm orientations across the 3 behavioral epochs for PMd (*A–C*) and area 5 (*D–F*) cells. Changes in arm orientation resulted in correlated changes in cell discharge before, during, and after movement. Axes show the average discharge level (spikes/s) of the cell for a given behavioral epoch. Two intersecting diagonal lines are the regression lines for ordinate on abscissa and abscissa on ordinate.

of changes in directional tuning between RT + MT and THT for MI cells ($r = 0.40$, $P < 0.01$) (Scott and Kalaska 1997).

The RT + MT epoch in this study starts when the target light is illuminated and finishes at the end of limb movement. It might be argued that changes in cell activity between arm orientations, as described above, may be largely the result of afferent feedback from the periphery during movement. To address this issue, we analyzed three 200-ms time periods within the RT + MT epoch: the 200 ms before movement onset, the 200 ms after movement onset, and from 200 to 400 ms after movement onset. For cells directionally tuned in both arm orientations, the average change in directional tuning for the three time periods was 23.2° ($n = 139$), 29.0° ($n = 156$), and 26.8° ($n = 126$), respectively, confirming that cell tuning was altered both before and during movement. There was a tendency for cells to show slightly smaller changes in their directional preference before movement onset than after. A more detailed analysis on the temporal variations in cell directionality between the two arm orientations is beyond the scope of the present article (Scott and Kalaska 1996).

DISTRIBUTION OF PREFERRED DIRECTIONS. The distribution of preferred directions of PMd cells were distributed uniformly for both arm orientations during the THT epoch and for the abducted arm orientation during the RT + MT epoch ($P > 0.05$, Rayleigh test, Fig. 7). However, the distribution for the natural arm orientation during RT + MT was not uniform ($P < 0.01$) but bimodal with a major axis oriented at 167–347°. Analysis of the distribution of preferred directions for each hemisphere demonstrated that this bimodality was generated by a highly nonuniform ($P < 0.001$) and bimodal distribution for the 67 cells recorded in the left hemisphere in the first monkey. In contrast, the distribution for the other three hemispheres combined was uniform ($P > 0.10$). The very strong bimodal distribution observed for the left hemisphere of the first monkey may reflect partially the fact that penetrations in this hemisphere were clustered more tightly than in the other hemispheres resulting in an inadvertent sampling bias for the directional tuning of PMd cells in that hemisphere (see Fig. 1).

VARIATION IN CELL ACTIVITY BETWEEN REPLICATED DATA FILES. Because neuronal activity was recorded first in one arm orientation and then in the other, any arm orientation effect on cell discharge will be confounded by possible systematic temporal variability in the activity of the cell. A second set of data files was collected for some cells, and the responses of the cells in the duplicated data files in the same arm orientation were compared. A total of 34 duplicate files (19 natural and 15 abducted) were recorded in PMd. There was a significant change in the level of discharge during CHT for only 4/34 (12%) replicated files (F test, $P < 0.01$, Table 1, Fig. 8), and the average absolute change in cell discharge was only 1.8 spikes/s (Fig. 8). The magnitude of change in discharge between replicated files was statistically smaller than the observed change of these same cells between arm orientations (3.3 spikes/s; $P < 0.001$, paired t-test) and smaller than observed for the entire cell sample (3.9 spikes/s; $P < 0.001$, Wilcoxon-Mann-Whitney test). Changes in the mean level of discharge during RT + MT

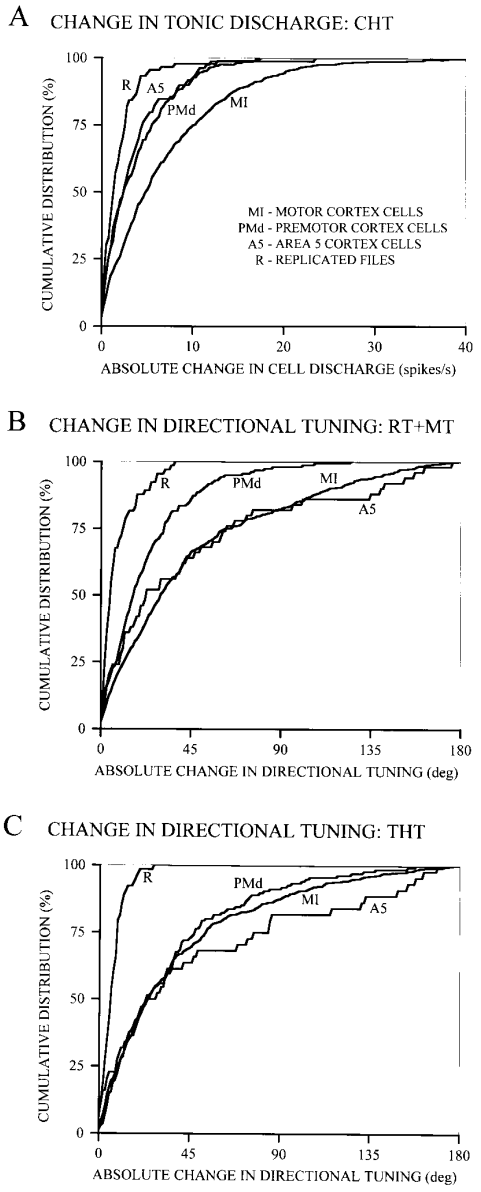

FIG. 5. *A*: cumulative frequency distribution (CFD) of the change in cell discharge between arm orientations observed during CHT for PMd, MI, and area 5 cortical regions. *B* and *C*: CFDs for the absolute change in directional tuning of cells in each cortical region for movement [combined reaction time and movement time (RT + MT)] and posture [target hold time (THT)]. Also shown are the CFDs for changes in the response of cells in PMd and MI between replicated (R) files using the same arm orientation.

and THT were found for only five (15%) and two (6%) replicated files, respectively ($P < 0.01$).

Only four (12%) and two (6%) cells showed a statistical change in their directional signal between replicated blocks of trials during RT + MT and THT epochs, respectively (F test, task × direction interaction, $P < 0.01$). A statistical difference in the directional preference of pairs of replicated files was observed only once (4.9%, Watson-Williams test, $P < 0.01$, Table 1), and the average absolute shift in directional tuning between pairs of duplicate files was only 9.7° (Fig. 8). The average absolute change in directional tuning between replicated files was statistically smaller than their

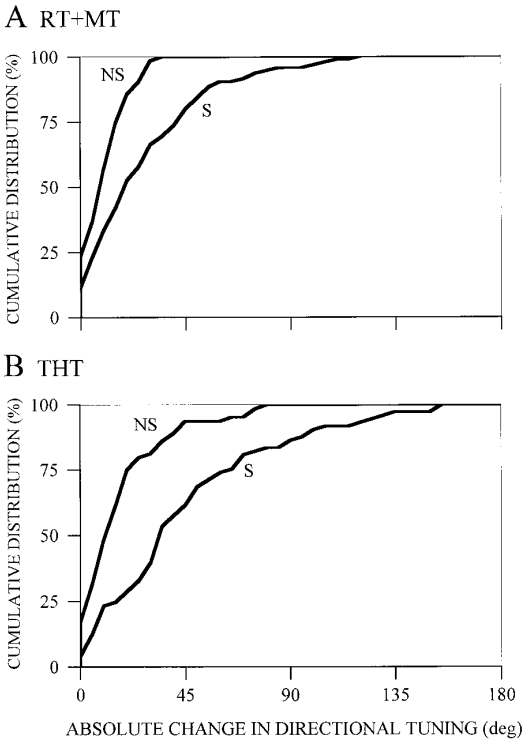

FIG. 6. Cumulative frequency histograms of the distribution of changes in directional tuning of PMd cells that were directional in both arm orientations but showed a significant (S) or nonsignificant (NS) task × direction interaction effect (analysis of variance, $P < 0.01$) during the RT + MT (*A*) or THT (*B*) epochs.

observed change in directionality between arm orientations (28.6°; nonparametric test for dispersion, $P < 0.01$) and smaller than the observed change in directionality for the entire cell sample ($P < 0.01$). Similar results were found for the THT epoch; there were no statistical differences in

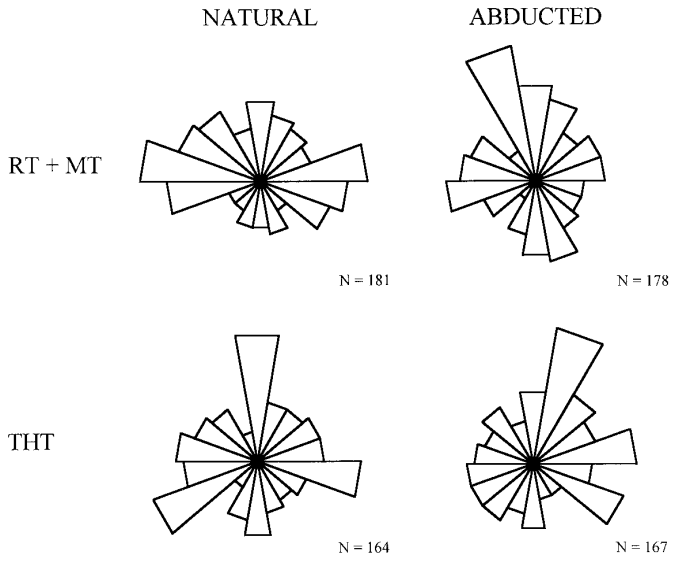

FIG. 7. Frequency distribution of the preferred directions of PMd cells that were tuned directionally during RT + MT and THT epochs in the natural and abducted orientations. Number of cells with a preferred direction within each 20° region is proportional to the length of the corresponding segment.

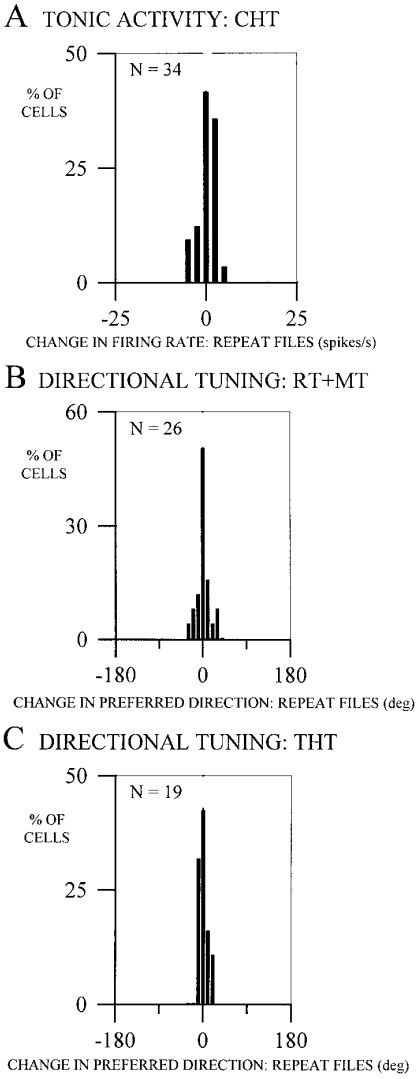

FIG. 8. Change in activity of PMd cells between repeated files using the same arm orientation. *A*: change in the tonic level of discharge during CHT. *B* and *C*: change in directional tuning of cells between repeated files during RT + MT and THT, respectively. Format same as Fig. 3.

the directional preference of cells between pairs of replicated files (Watson-Williams test, $P < 0.01$), and the average absolute change in directional tuning between duplicate pairs of files was only 6.8°.

The stability of cell responses in PMd for replicated movements in a given arm orientation was statistically similar to that observed for MI cells (change in discharge level, $P > 0.05$, Wilcoxon-Mann-Whitney test; change in directionality, $P > 0.05$, nonparametric test for dispersion). For comparison purposes, the response of cells recorded in replicated files from both MI and PMd are combined to generate a single cumulative distribution for the absolute change in firing rate and absolute change in directional tuning for replicated files (Fig. 5). Figure 5 illustrates that cell activity in a given arm orientation remains relatively stable between replicated files, and thus temporal changes in the activity of cells cannot explain the large changes in the activity of cells between arm orientations in either PMd or in MI.

RESPONSE TO PASSIVE LIMB MOVEMENTS. In our previous study on MI cell activity during reaching, we found that the majority of cells responded to passive movement of the shoulder and/or elbow joints (461/534, 86% of cells) (Scott and Kalaska 1997) and that there were some significant differences in the task-related activity of elbow- and shoulder-related cells. We attempted a similar analysis for PMd cells, but found that only 75/152 (49%) of tested cells responded to passive movement of the proximal joints, which is significantly less than observed in MI ($P < 0.01$, χ^2 test). Further, the response of PMd cells to passive limb movements were qualitatively weaker, more variable, and more difficult to localize with confidence than was the case in MI. Because of the uncertainties and low success rate in identifying peripheral receptive fields in PMd, we did not attempt a comparison of the behavior of cells with sensory input from the shoulder versus the elbow.

Variation in cell activity in area 5

CHANGES IN DISCHARGE LEVEL. For area 5, 28/79 cells (35%) showed changes in their tonic level of activity during CHT between arm orientations (Table 1; Fig. 9*A*). Average absolute change in tonic activity was 3.6 spikes/s, but the average level of discharge of cells in the two arm orientations was similar (9.3 and 9.9 spikes/s for natural and abducted orientations; paired *t*-test, $P > 0.10$). Slightly higher percentages of cells showed changes in the grand mean of activity during RT + MT (51%) and THT (50%) epochs between arm orientations. Change in cell activity between orientations also tended to be coupled between the three behavioral epochs (Fig. 4, *D–F;* CHT vs. RT + MT, $r = 0.66$; CHT vs. THT, $r = 0.80$, and RT + MT vs. THT, $r = 0.81$; $P < 0.01$ for all). In general, arm orientation had a less pronounced effect on the tonic level of discharge of Area 5 cells as compared with MI (Fig. 5*A*).

CHANGES IN DIRECTIONAL TUNING. Most cells in area 5 (89%) displayed a significant task × direction interaction in their response to movements in different directions during either RT + MT or THT, and often in both (*F* test, $P < 0.01$, Table 1). As with PMd cells, this effect reflected either a change in the sharpness of cell tuning or a change in its directional tuning and often in both. For RT + MT, 50/79 cells (63%) were directionally tuned in both arm orientations, but 8 and 11 cells were identified as unimodally tuned only in the natural and abducted orientations, respectively (bootstrap test for directionality, $P < 0.01$). Ten cells were not directionally tuned in either orientation during RT + MT epoch; 26/50 (52%) cells directionally tuned in both orientations showed a significant task × direction interaction effect, and 6 (23%) of these cells with a significant interaction effect also showed a significant change in their dynamic range (*t*-test, $P < 0.01$).

Of those cells directionally tuned in both orientations, the directional preference of 20/47 cells (43%) were significantly different between the two orientations (Watson-Williams test, $P < 0.01$, 3 cells could not be analyzed with this test, Fig. 9*B*). As seen in PMd and MI, some cells in area 5 showed only a small directional shift between orientations, whereas other cells showed almost a 180° difference in their directional signal between orientations. The average absolute

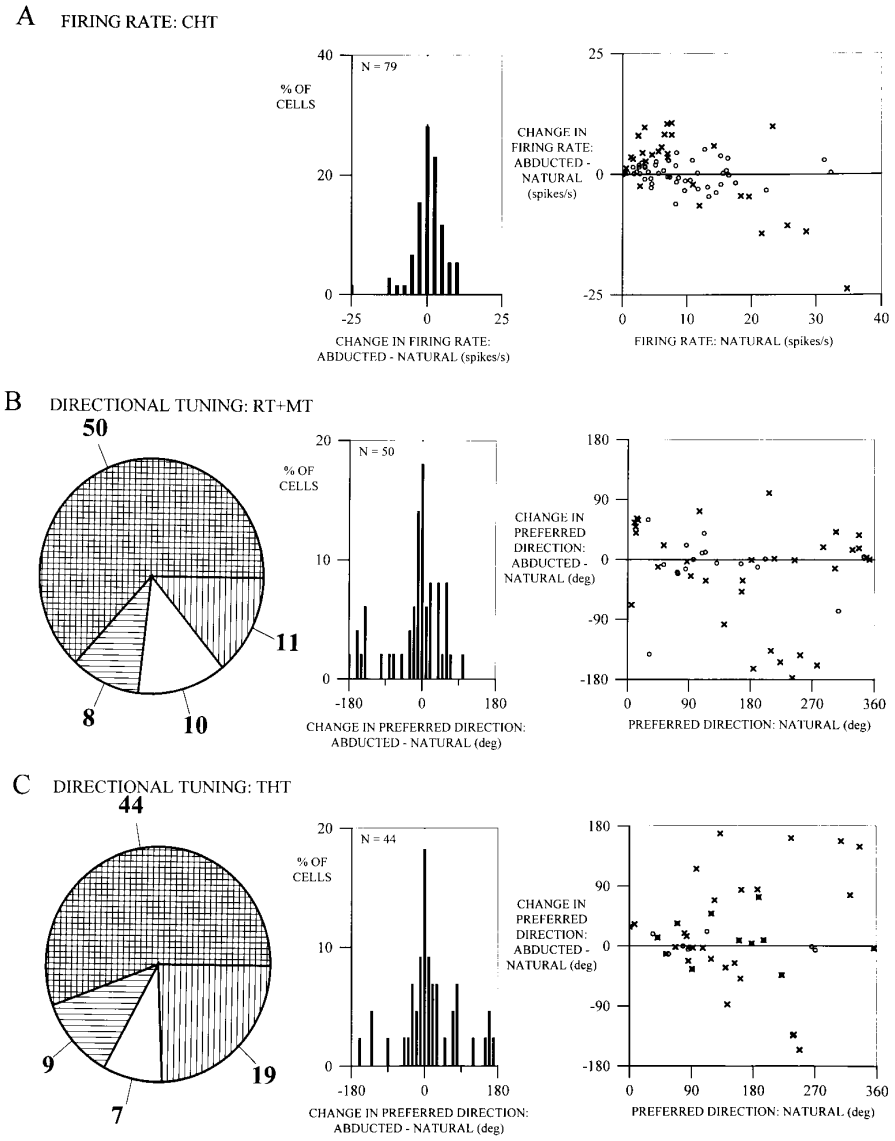

FIG. 9. Changes in the activity of area 5 cells during reaching movements in different arm orientations. *A*: change in the tonic level of cells during CHT between orientations. *B* and *C*: changes in the directional tuning of cells during RT + MT and THT, respectively, between orientations. Format of diagram same as Fig. 3.

shift in directional tuning between orientations for RT + MT was 46.2°, whereas the average change in directional tuning (arithmetic mean) across all cells was −16.4° clockwise. Although area 5 cells tend to be active later than PMd cells, changes in arm orientation altered the directional preference of these parietal cells both before and during movement. We analyzed the directional preference of area 5 cells for the same three 200-ms time periods within the RT + MT epoch as performed on PMd cells. For cells directionally tuned in both arm orientations, the average absolute directional shift was 37.6° ($n = 24$), 45.2° ($n = 50$), and 55.3° ($n = 53$), respectively. As observed in PMd, changes in directional tuning tended to be smaller before as compared with during movement.

Changes in the relationship between cell activity and movement direction of area 5 cells during THT were similar to those observed during RT + MT, described above, including modulation of the sharpness and preference of cell tuning. Thirty-one of 44 cells (70%) showed a significant task × direction interaction effect, and 12 (27%) of these cells showed a significant change in their dynamic range (*t*-test, $P < 0.01$). Almost half the cells (41%) that were directionally tuned for both arm orientations showed a statistically significant change in tuning between orientations (Watson-Williams test, $P < 0.01$, Table 1). The average absolute shift in directional tuning between arm orientations was 48.4°, whereas the arithmetic mean was 13.8° counterclockwise (Fig. 9*C*). As seen in PMd, there was no correlation between changes in the directional tuning of cells for RT + MT and THT ($r = 0.08$, $P > 0.05$).

DISCUSSION

A major focus of motor research has been to understand the nature of the putative neuronal representations and transformations presumed to be performed by the CNS to convert retinal signals of target location into motor output to muscles to move the hand to the target (Georgopoulos 1991; Kalaska 1991a, 1995; Kalaska and Crammond 1992; Soechting and Flanders 1992). A key step in this process involves the

conversion of signals related to the global goal of the task into signals related to the mechanical details of movement, such as from extrinsic variables related to target location and motion of the hand toward the target into intrinsic variables related to motion of the intervening limb segments and to muscle activity. We have developed a paradigm to separate these two classes of variables by training monkeys to make reaching movements using similar hand trajectories but different arm orientations. A previous study demonstrated that neuronal activity in MI was sensitive to changes in arm orientation during reaching movements (Scott and Kalaska 1997). These results argue that the activity of most cells in MI during reaching is not simply related to target location or hand trajectory but is modulated strongly by attributes of movement that vary with arm geometry. The present study expands on those initial findings by demonstrating that both the level of tonic discharge and the task-related directionality of cells in PMd and parietal area 5 also are influenced by arm orientation before, during, and after movement. In general, the proportion of cells that showed a change in activity between arm orientations and the magnitude of this change was less in PMd than in MI, particularly during RT + MT. The effect of arm orientation on the response of area 5 cells tended to be intermediate to that observed in PMd and MI, but the area 5 sample size is too small to make stronger statements.

Dorsal premotor cell activity is sensitive to changes in arm orientation during movement and posture

The present results demonstrate that the activity of single PMd cells does not appear to exclusively reflect extrinsic variables of the task because the activity of a majority of cells in this motor region was sensitive to changes in arm orientation during movement and while maintaining constant hand locations. These results are not an artifact of changes in cell responsivity over time because there were minimal differences in the activity of cells between replicated files when reaching movements were performed using the same arm orientation (Fig. 8). As well, the hand trajectories overlapped extensively when movements were performed using the two arm orientations. Although neuronal activity could reflect other variables related to hand path, such as movement velocity, these factors generally have a smaller effect on cell activity as compared with movement direction (Schwartz 1992). Furthermore, the effect of arm orientation on the directionality of cells in PMd was greater when the monkey was holding its hand stationary over the peripheral targets as compared with during movement. Under these conditions of stable arm postures, it is difficult to explain the changes in the level of activity or in the directional tuning of cells between arm orientations as arising from differences in the spatial kinematics of hand motion and hand location (see also Scott and Kalaska 1997).

Even though cell activity in PMd was less sensitive to changes in arm geometry than cell activity in MI, it is possible that both of these neural representations are intrinsic in nature but represent different sets of intrinsic parameters. This notion can be illustrated by the observed differences in the effect of arm orientation on the task-related directionality of cell-like units in two mathematical models that encode different intrinsic features of the task, either changes in joint angle or joint torque (Scott and Kalaska 1997). On average, units that encode changes in joint angle changed by 33° when reaching movements were made using different arm orientations, whereas units that encode changes in joint torque changed by 64°. A reduction in the effect of arm orientation on the directionality of units in the joint kinematic model as compared with the joint torque model did not reflect an increase in information related to the extrinsic features of movement. Rather, these differences demonstrate that arm geometry does not influence equally the mapping between extrinsic hand-based coordinates and each intrinsic coordinate frame. Correspondingly, it is possible that differences in the sensitivity of PMd and MI cells reflect differences in the effect of arm orientation on the mapping from their respective intrinsic representations to hand movement direction.

Alternatively, differences in the effect of arm orientation on PMd and MI activity may suggest that the discharge of cells in these precentral cortical regions reflect both extrinsic and intrinsic features of the task but to differing degrees. Cell activity in PMd would express to a greater degree the extrinsic attributes of the movement, whereas MI would reflect a greater prominence of intrinsic parameters. This still would be consistent with hypotheses that PMd tends to be concerned with more higher-order processes than MI (di Pellegrino and Wise 1991, 1993; Kurata 1993; Mitz et al. 1991; Okano and Tanji 1987; Shen and Alexander 1997a,b; Weinrich and Wise 1982; Wise et al. 1996) and that such processes are more concerned with extrinsic variables of the task, such as hand trajectory (Flash 1987; Gordon et al. 1994; Morasso 1981).

The increased importance of extrinsic information in the discharge patterns of cells in PMd is consistent with recent studies that dissociated the direction of forelimb movement from the spatial location of the visual cues (Shen and Alexander 1997b). They found that activity in MI before and especially during movement, predominantly, but not exclusively, was related to movement direction rather than to target direction. In PMd, the reverse was true; cell activity was related more often to target direction. Further, neuronal activity in PMd can be modulated by spatial attention (Boussaoud and Wise 1993; di Pellegrino and Wise 1993) and even by signals related to the localization of the spatial target, such as gaze angle (Boussaoud 1995). Although this gaze-related activity was only observed before movement when the monkey waited for a go signal, neuronal activity in PMd also may reflect this extrinsic feature of the motor task during the execution of movement (Jouffrais and Boussaoud 1996).

For heuristic purposes, the transformation of visual target information into motor output of muscles often is described as a series of transformations converting information between distinct coordinate systems derived from geometric or newtonian variables, such as hand kinematics or joint angles or torques (Kalaska 1991a, 1995; Kalaska and Crammond 1992; Soechting and Flanders 1989, 1992). However, the observed effects of such diverse factors as gaze angle (Boussaoud 1995; Wise et al. 1996), target direction (Shen and Alexander 1997b), and arm orientation (present study) on the discharge pattern of cells in PMd suggests that the

sensorimotor transformations related to visually guided reaching movements may involve a gradual conversion of signals, from higher levels that reflect more extrinsic information to lower levels that reflect more intrinsic features of the task. This gradual conversion would create a shift in the frequency and strength of observed neural discharge correlates with various intrinsic and extrinsic features of the movement between different cortical regions (Shen and Alexander 1997a,b). Further, there appears to be no abrupt anatomic or functional border between MI and PMd (Crammond and Kalaska 1996; He et al. 1993; Johnson et al. 1996; Weinrich and Wise 1982). Therefore, it appears more appropriate to talk of a rostrocaudal gradient in the information processed by individual cells across the precentral cortex with more extrinsic information in rostral PMd and more intrinsic information related to the moment-to-moment details of motor output in caudal MI in the bank of the sulcus (Crammond and Kalaska 1996; Johnson et al. 1996).

The information conveyed by the discharge pattern of cell populations, or even of single cells, in different cortical areas also may vary with time during a behavioral task (Ashe and Georgopoulos 1994; Fu et al. 1995; Zhang et al. 1997). For instance, Shen and Alexander (1997a,b) report that there was a progressive decrease in the strength of neuronal correlates of higher-order visuospatial aspects of a task in both PMd and MI accompanied by a progressive increase in neuronal correlates of the details of the implementation of the motor response. In our study, the directionality of cells in PMd was more sensitive to changes in arm orientation after movement when the monkey maintained a constant arm posture at the peripheral targets as compared with during movement. This also could be interpreted as evidence of a progressive shift in PMd activity from more extrinsic to more intrinsic information between the movement and target-hold phases of the task.

The proportion of cells showing changes in activity with arm orientation and the magnitude of these changes in PMd were clearly smaller than observed in MI. Initially, this appears to contradict observations by Caminiti et al. (1991), who reported that the directionality of cells in both PMd and MI rotated or covaried with initial shoulder joint angle when reaching movements were performed in different parts of space. This similarity between PMd and MI was interpreted as evidence that a common arm-centered coordinate frame was present in these two cortical regions (Caminiti et al. 1991). However, the representations in these two cortical areas could have similar origins but different coordinate frames. Furthermore, the tuning of cells related to target location or movement direction of the hand in body-, head-, or eye-centered coordinate frames all will tend to rotate systematically when reaching movements are performed in different parts of space. Under the definitions used in the present study, such target or hand-related information would be extrinsic variables because they do not explicitly specify or depend on the geometry of the limb only on the spatial location of the target or hand relative to the origin of the coordinate frame. The present paradigm dissociated variables that depend on the geometry of the limb (intrinsic) from those that do not (extrinsic) by training monkeys to make reaching movements using similar spatial trajectories but with different arm orientations. Therefore extrinsic variables remained relatively constant, whereas intrinsic variables tended to rotate about an axis passing through the shoulder and hand when movements were performed in the abducted as compared with the natural arm orientation. This change in arm geometry had a greater influence on MI as compared with PMd activity, suggesting a significant difference in the information processed in these two precentral motor regions with extrinsic variables more prominent in PMd and intrinsic parameters predominating in MI. This is also consistent with the findings of Shen and Alexander (1997b), who reported that PMd activity was proportionately more related to visuospatial aspects and MI activity related more to the motor output during the task.

Finally, we must acknowledge that the modulation of cell activity by arm posture is not unambiguous proof that the cells are signaling the covariation of intrinsic movement parameters with movement direction. It is possible that cell activity reflects a hybrid coordinate frame encompassing both intrinsic and extrinsic features of the task (Lacquaniti et al. 1995). For example, task-related discharge of the cells may covary with the extrinsic parameter of movement direction, but in a coordinate frame the axes of which rotate with the geometry of the arm, such as the plane formed by the upper arm and forearm. However, such a coordinate frame becomes ill defined when the arm is fully extended. Further, because the rotation of the plane of the arm in our task was orthogonal to the plane of the task, some cells with preferred directions to the left and right would show a 180° change in their preferred directions. As shown in our results (Figs. 3 and 5), no PMd cells displayed a complete reversal in their preferred directions. In general, it would be very difficult to distinguish between many hybrid and intrinsic coordinate systems (Lacquaniti et al. 1995), illustrating the imposing difficulties that still remain in trying to discern the nature of the relationship between cell discharge and different movement parameters.

Parietal area 5 neuronal activity and arm orientation

A previous attempt to identify the nature of the neuronal representation of movement and posture in area 5 was performed by Lacquaniti et al. (1995) when they studied the response of cells in this cortical region during reaching movements in different parts of space. Regression analysis techniques were used to relate neuronal activity to several different reference frames that were based on either extrinsic variables related to the position of the hand in space or intrinsic variables related to the specific orientation of the limb segments. Although their results showed that the best coordinate frame to interpret neuronal activity in area 5 was body-centered, they found relatively small differences in the predictive power of the various extrinsic and intrinsic coordinate systems. This inability to identify the best representation to interpret the activity in area 5 is at least partially due to the stereotypical coupling between different variables during highly practiced natural movements (Lacquaniti et al. 1995).

Our observation that neuronal activity in area 5 was sensitive to changes in arm orientation during movement and posture is inconsistent with models based only on extrinsic features of the motor task (Ashe and Georgopoulos 1994; Lacquaniti et al. 1995). Of the four different coordinate

frameworks tested by Lacquaniti et al., only the frameworks using the angle of limb segments, based on work by Soechting and Flanders (1989), would predict changes in neuronal activity between the natural and abducted arm orientations analyzed in this study. Although the present results support the notion that the neuronal representation in area 5 is modulated by intrinsic features of movement, the limited data sample cannot adequately identify whether any one coordinate frame is better than another.

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Address reprint requests to J. F. Kalaska.

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