Modest Gaze-Related Discharge Modulation in Monkey Dorsal Premotor Cortex During a Reaching Task Performed With Free Fixation

PAUL CISEK AND JOHN F. KALASKA
Centre de Recherche en Sciences Neurologiques, Université de Montréal, C.P. 6128, Succursale Centre-ville, Montreal, Quebec H3C 3J7, Canada

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Cisek, Paul and John F. Kalaska. Modest gaze-related discharge modulation in monkey dorsal premotor cortex during a reaching task performed with free fixation. J Neurophysiol 88: 1064–1072, 2002; 10.1152/jn.09951.2001. Recent studies have shown that gaze angle modulates reach-related neural activity in many cortical areas, including the dorsal premotor cortex (PMd), when gaze direction is experimentally controlled by lengthy periods of imposed fixation. We looked for gaze-related modulation in PMd during the brief fixations that occur when a monkey is allowed to look around freely without experimentally imposed gaze control while performing a center-out delayed arm-reaching task. During the course of the instructed-delay period, we found significant effects of gaze angle in 27–51% of PMd cells. However, for 90–95% of cells, these effects accounted for <20% of the observed discharge variance. The effect of gaze was significantly weaker than the effect of reach-related variables. In particular, cell activity during the delay period was more strongly related to the intended movement expressed in arm-related coordinates than in gaze-related coordinates. Under the same experimental conditions, many cells in medial parietal cortex exhibited much stronger gaze-related modulation and expressed intended movement in gaze-related coordinates. In summary, gaze direction-related modulation of cell activity is indeed expressed in PMd during the brief fixations that occur in natural oculomotor behavior, but its overall effect on cell activity is modest.

INTRODUCTION

Neurophysiological studies of arm movement-related cell discharge in premotor cortex have been conducted for many years (Wise 1985). Cells in dorsal premotor cortex (PMd) discharge in relation to several parameters of reaching movements, including direction (Alexander and Crutcher 1990; Caminiti et al. 1991; Crammond and Kalaska, 2000; Crutcher and Alexander 1990; di Pellegrino and Wise 1993; Kalaska and Crammond 1995; Messier and Kalaska, 2000; Scott et al. 1997; Shen and Alexander 1997) and extent (Fu et al. 1993; Kurata 1993; Messier and Kalaska, 2000; Riehle and Requin 1989), and they are clearly more related to movement planning than to attentional or sensory processing (Boussaoud and Wise 1993; di Pellegrino and Wise 1993; Wise et al. 1992). Taken together such results strongly argue for a role of arm regions of premotor cortex in the planning and execution of reaching movements (Kalaska et al. 1997; Wise 1985; Wise et al. 1997).

In most of those studies, the head-fixed animals were allowed to look around freely, under the assumption that gaze behavior did not affect the arm-related cell activity being recorded. However, Boussaoud et al. (1993) showed that, when monkeys were trained to maintain fixation in different directions and to release a switch in response to the onset of a visual stimulus, cell discharge in premotor and prefrontal cortex was modulated by the angle of gaze. Later it was observed that gaze angle also modulated arm movement-related cell discharge in ventral premotor (PMv) (Mushiake et al. 1997) and dorsal premotor cortex (PMd) (Boussaoud et al. 1998; Jouffrais and Boussaoud 1999). Furthermore, during the performance of an instructed-delay saccade task, intracortical microstimulation of the rostral part of PMd was found to produce eye movements whose metrics were specific to the site of stimulation (Fuji et al., 2000). Strong gaze direction-related activity modulation has also been reported in a medially located “parietal reach region,” where reach-related directional tuning was systematically better in gaze-centered than in hand-centered coordinates (Batista et al. 1999).

These findings raise several questions. First, in all studies of gaze-related modulation to date, monkeys were trained to fixate specific locations in space for extended periods of time. However, during natural behavior, primates make frequent saccadic eye movements that briefly fix gaze on various objects of interest. Does gaze-related modulation appear in PMd during such unconstrained natural behavior? Second, how strong is the effect of gaze-related modulation during free gaze compared with the well-documented arm movement-related activity in PMd? Third, does gaze-related modulation imply that intended movement direction is represented in PMd in gaze-related coordinates rather than in arm-related coordinates?

These findings also raise the question as to what degree gaze-related modulation may have confounded previous published reports of PMd arm movement-related discharge during tasks in which oculomotor behavior was not controlled or monitored. For example, Caminiti et al. (1991) reported that the directional preferences of premotor cells shift as a monkey...
makes movements in different parts of space, and this influential result has been used to argue that movements are represented in PMd using an intrinsic arm-related coordinate system (Ajemian et al., 2000; Caminiti et al. 1991; Sanger 1994). However, Boussaoud et al. (1998) suggested that the observed shift may be due to a shift in gaze direction, implying instead a head-centered or gaze-centered coordinate system. Other results, including neural sensitivity to movement extent (Fu et al. 1993; Kurata 1993; Messier and Kalaska, 2000; Riehle and Requin 1989), might also be subject to similar interpretation difficulties.

In this study we analyze the effect of gaze direction on cell discharge in PMd during a reaching task in which a monkey is allowed to look around freely. Some of these results have previously appeared in abstract form (Cisek and Kalaska, 2000).

**METHODS**

**Behavioral task**

A monkey (*Macaca mulatta, 6 kg*) performed a center-out reaching task using a manipulandum moving in the horizontal plane to control a cursor on a screen located 48 cm away at eye level (Fig. 1A). The monkey began each trial by placing the on-screen cursor within a central circle (1.5-cm radius) for a 500-ms center-hold-time (CHT). Next, a cue circle (2-cm radius) appeared in one of eight possible target locations on the circumference of an 8-cm radius circle, for a cue period (CUE) lasting 1,000 ms. The cue then disappeared for a memory period (MEM) lasting from 1,500 to 4,000 ms. Finally, the central circle disappeared and eight identical circles (2-cm radius) appeared at the eight peripheral locations. This GO signal instructed the monkey to move to the location of the cued target. The reaction time (RT) was defined between the GO signal and movement onset (232 ± 60 ms, mean ± SD), and movement-time (MT) was defined between movement onset and offset (449 ± 97 ms). These together defined the reaction + movement time (RTMT) period. To receive a liquid reward, the monkey had to hold the cursor within the correct cued target for a target-hold-time (THT) of 1,000 ms. Trials were presented in a randomized-block sequence until 6–10 correct reaching movements were made to each of the eight targets. Gaze was unconstrained and eye movements were measured at 100 Hz using a Bovis infrared oculometer (Karlsruhe).

**Cortical recording**

Recording chambers were implanted surgically under inhalation anesthetic, and conventional techniques were used to isolate and record single-unit activity from the cerebral cortex. All procedures

![Fig. 1. A: behavioral task. Circles indicate cues present during different task periods. Cross indicates the location of the on-screen cursor. B: gaze direction projected onto the screen workspace during fixation episodes in the different task periods, collected from all trials in which the target was at the top right. Circles indicate the locations of the central circle and the 8 movement targets (although these are not visible during all periods). Note that during the CUE and MEM periods, the monkey looks around but tends to look toward the cued target location. During RTMT, the monkey typically fixes the target before moving the cursor toward it. The same trends in oculomotor behavior were observed in trials with cued targets in the other 7 locations. C: locations of penetrations made in PMd and medial parietal cortex. Size of circles is proportional to the number of cells recorded. IHF, interhemispheric fissure; CS, central sulcus; IPS, intraparietal sulcus; AS, arcuate sulcus; PS, principal sulcus.](http://jn.physiology.org/doi/10.1152/jn.01278.2001)
followed university and national guidelines for animal care. Figure 1C illustrates the locations of the premotor and parietal penetrations where cells included in this report were recorded.

Data analysis

Cells were examined if they exhibited task-related changes of activity and showed arm movement-related directional preferences in at least one task period. Each cell’s mean discharge rate (including partial spike intervals) was calculated for every period of every trial. For each cell, a directional tuning function was calculated for every period by averaging the activity across all trials with movements toward each of the eight directions. The preferred direction (PD) of each cell in every period was calculated using trigonometric moments. Tuning functions were tested for unimodal directionality using a nonparametric bootstrap test (Georgopoulos et al. 1988) with 1,000 repetitions and a criterion of $P < 0.01$.

Instantaneous eye movement speed throughout each trial was calculated at 10-ms intervals by differentiation of the oculometer signals. Fixation episodes were identified as time periods of $\geq 100$ ms during which eye speed did not exceed 2.4 times the SD of the speed distribution computed over the entire trial. The average gaze direction was determined for each fixation episode and the average spike rate computed from the portion of each episode that fell within the task period of interest (CHT, CUE, MEM, and RTMT) after the first 50 ms was excluded to avoid potential confounds of perisaccadic activity.

For each cell, gaze-related modulation was studied separately during CHT, CUE, MEM, and RTMT periods using two kinds of analyses: 1) analysis of variance (ANOVA) to determine significant gaze effects and 2) planar regression (Boussaoud et al. 1998) to determine the strength and form of gaze effects. First, a one-way ANOVA was used to compare cell activity during five groups of fixations: those that fell within 4.5° of the center of the workspace and those that fell within 4.5° of four peripheral locations 9° to the upper-right, upper-left, lower-right, and lower-left of the center. These locations corresponded to four of the eight arm movement targets and were chosen to facilitate comparison with the data of Boussaoud et al. (1998), who used similar gaze-fixation locations.

Second, a “gaze-direction” planar regression was performed separately on all the fixation episodes, expressing spike rate during each fixation as a function of the horizontal and vertical components of gaze direction (Boussaoud et al. 1998). The strength of the effect of gaze direction on cell activity was characterized using the $R^2$ value of the regression and the slope of the best-fit plane along its gradient (i.e., the square root of the sum of squares of the horizontal and vertical slopes). Two additional variations of gaze-direction regressions were performed. First, a planar regression was performed excluding activity during those fixations that fell within 6° of the target of each given trial. Second, a planar regression was performed for each cell using data only from trials toward the target nearest to the cell’s arm movement-related PD and the adjacent targets on either side. The rationale behind these analyses is described in RESULTS.

Finally, to investigate whether gaze-related modulation could have been responsible for the PD shifts observed by Caminiti et al. (1991), we collected arm-related directional tuning functions using two separate subsets of data: 1) cell discharge from trials in all eight directions but only while the monkey fixated within 6° of the center of the target display and 2) cell discharge from trials in all eight directions but only while the monkey fixated within 6° of a peripheral location 18° to the left of the center. These locations are similar to the centers of two of the three workspace regions used by Caminiti et al. (1991) and allow comparison of tuning function shifts with the shifts observed in that study.

RESULTS

Eye movements

During the performance of the reaching task, the monkey made numerous eye fixations with a median duration of 420 ms (the mode of the duration distribution was 240 ms, $n = 103,342$). As illustrated in Fig. 1B, these fixations were distributed over a wide region of space (95% of the fixations fell within a region which spanned 53° horizontally and 37° vertically) but were particularly concentrated near the central target, near the intended target locations, near a leftward location (toward the door of the recording room), and near a rightward location (toward the experimenter).

Because of the strong coupling of gaze direction with hand target location during RTMT (Fig. 1B), gaze-related modulation found during this period cannot be separated from a cell’s arm movement-related directional tuning. For this reason, we do not focus our analyses on this task period. In contrast, fixation behavior and cell activity during CHT is completely independent of the upcoming arm movement, and provides an unbiased estimate of gaze-related modulation. However, during CHT, cell activity and discharge variability tend to be low. Fixations during the CUE and MEM periods cover a wide range of visual space, allowing for the most meaningful regressions of cell activity against gaze direction. However, because of the animal’s tendency to perform more fixations toward the intended movement target, estimates of gaze-related modulation may be confounded by the presence of directional tuning with respect to arm movement. For this reason, an additional planar regression was performed during the MEM period which excluded fixations within 6° of the intended movement target for each trial. This provided an estimate of gaze-related modulation that was not confounded by the overt coupling between gaze direction and the intended target.

Cell activity

Oculometer data were obtained during recordings from 73 cells in PMd. Of these, 50 were unimodally tuned to the intended arm movement direction during the CUE period (68%), 69 were tuned during the MEM period (95%), and 71 were tuned during either RT or MT (97%). For most of these cells, the PD was similar throughout the CUE, MEM, and RT periods. For some, directional tuning during MT was opposite
to their tuning during RT (Fig. 2, A and B). For comparison, single-unit recordings were also made from 35 cells in the superior parietal cortex, including the medial portion of area 5.

Gaze-related modulation in PMd

According to the ANOVA, gaze-related modulation occurred in about 1/3 of PMd cells during the CHT and CUE periods and in about 1/2 of cells during the MEM period (Table 1). Comparable results were obtained when the ANOVA was performed using fixations near the center and targets 9° to the right, left, above, and below the center. For most of these cells the strength of this modulation was rather modest, as shown by the planar regression analyses (Table 2). The three kinds of analyses performed on data during the MEM period yielded very similar results.

Two examples of PMd cells are shown in Fig. 2, A and B. Both of these were significantly tuned (bootstrap test, $P < 0.01$) to the direction of intended arm movement. The cell shown in 2A is a typical PMd cell with a burst at cue onset and sustained discharge during the CUE and MEM periods when the target is near its preferred direction (Crammond and Kalaska, 2000). Although this cell showed statistically significant gaze-related modulation (ANOVA, $P < 0.05$), the effect of this modulation was quite small. During CHT, the slope of the best-fit regression plane was 0.06 Hz/° and accounted for

**FIG. 2.** Cell data. A: typical cell in PMd. Left: activity during trials toward the preferred (top) and opposite direction (bottom). Circular diagrams on the far left indicate cue location. For each direction, the first histogram is aligned on cue onset (C) and shows activity during the center hold time (CHT) and cue (CUE) periods and during the first 1,000 ms of the memory period (MEM). Thick marks in the rasters indicate cue onset and offset. The second histogram is aligned on movement onset (M), and shows activity during the end of MEM and during reaction and movement time (RTMT). Thick marks indicate the GO signal, movement onset, and movement offset. Circular diagrams above the histograms show the directional tuning functions during the different periods, and thick lines indicate the preferred direction (PD) of significant tuning. RT (dotted line) and MT (solid line) tuning functions are shown separately since they are oriented in opposite directions, as has been observed in some dorsal premotor cells (PMd) cells (Crammond and Kalaska 1996). Right: planar regressions of cell activity (Hz) against eye position. Top: the regression using fixation episodes during CHT; bottom: during MEM. This cell shows a weak effect of gaze direction. B: a second PMd cell, same format as A. This cell exhibits the strongest gaze effect found in the present sample of PMd cells. C: parietal cell exhibiting a very strong planar gaze effect. D: parietal cell exhibiting a spatially limited hemifield effect.
<1% of the variance of cell activity recorded during CHT fixation episodes. During MEM, the slope was 0.52 Hz° and gaze direction accounted for 15% of the variance. Thus this typical PMd cell exhibits a statistically significant but modest effect of gaze direction. In contrast, the slope of the regression of that cell’s activity during MEM against final hand location was 2.62 Hz° and accounted for 64% of the variance.

The cell shown in Fig. 2B exhibited the strongest gaze-related modulation observed in the present sample of PMd cells. During the CHT and MEM periods, gaze angle accounted for nearly one-half of the variance. Such cells, however, were quite rare (Table 2). In the population, only 11 cells (15%) had an $R^2$ value which exceeded 0.2 during the CHT period, and the median $R^2$ was 0.07. During the MEM period, the median $R^2$ was 0.04, and only 4 cells (6%) had an $R^2 > 0.2$. When the planar regression was repeated after excluding data from fixations within 6° of the intended movement target in each trial, the median $R^2$ value across the sample population was 0.07 (Table 2).

Examination of the slopes of the best-fit planar regressions also suggested that the strength of gaze-related modulation is low (Fig. 3A, and Table 2). For instance, the median slope during MEM was 0.16 Hz° (max = 0.61 Hz°). Boussaoud et al. (1998) observed that the strength of the gaze effect could vary with the direction of arm movement, being evident for some cells only in their preferred direction. By using data from trials in all 8 arm movement directions, our regression analysis may underestimate the true strength of gaze-related modulation in particular arm movement directions. Therefore we repeated the regression against gaze direction using only the trials in each cell’s preferred direction and the movement directions immediately adjacent to it. Discharge rates for these 3 adjacent movement directions are typically high and of fairly similar intensity, and so a regression using data from these directions will minimize any potential arm-related confound. This had only a minor effect on our results. The median slope during the MEM period was now 0.20 Hz° and the median $R^2$ value was 0.07. Repeating the gaze analysis for trials in each arm movement direction separately likewise had only negligible effects.

Comparison of gaze-related versus arm-related modulation

To compare the degree of PMd discharge modulation due to gaze-related versus arm-related variables, we compared the slopes and $R^2$ values of two planar regressions: “gaze-direction”, comparing activity during fixation episodes regressed against gaze direction; and “target-re-start“, comparing cell activity against final hand location relative to the start position (Fig. 3, B and C). During CHT, before target information is given, target-re-start slopes and $R^2$ values were very low, illustrating the range these values can take in the case of linear regressions performed against variables which cannot affect cell activity. Although several gaze-direction $R^2$ values were higher (Fig. 3C, Table 2), the gaze-direction slopes were low (Fig. 3B), in part because there was less discharge variance to be accounted for during CHT. After target information is given (CUE and MEM), the target-re-start slopes and $R^2$ values exceed the gaze-direction slopes and $R^2$ values for most PMd cells (the scatter-plots for CUE and MEM in Fig. 3, B and C are significantly below the diagonal identity line; paired t-test, $P < 0.01$), even though the monkey frequently looked at the intended target (Fig. 1B). During RTMT, when gaze is most strongly coupled to intended hand target (Fig. 1B), both gaze-direction and target-re-start slopes and $R^2$ values are large.

Comparison of arm-related versus gaze-related coordinates

The preceding analyses assessed the strength of the modulation of PMd activity as a function of momentary gaze direction and as a function of final hand position. Next, we performed a “target-re-gaze“ regression, re-analyzing the PMd activities during MEM as a function of final hand position in a gaze-centered coordinate system. That is, we performed a regression of cell activity during fixation epochs against the final hand position relative to the current gaze fixation location, i.e., a gaze-centered coordinate framework of reach planning (Batista et al. 1999). The $R^2$ values of this target-re-gaze regression (median $R^2 = 0.09$) were typically higher (paired t-test, $P < 0.01$) than the $R^2$ values of the gaze-direction regression (median $R^2 = 0.04$). Nevertheless, the PMd task-related discharge was still much better captured by an arm-related coordinate system (target-re-start) than a gaze-centered framework (target-re-gaze): the scatter-plot for PMd in Fig.

### Table 1. Number (and percent) of PMd cells with significant gaze-related modulation and PMd cells with significant arm movement–related directional tuning

<table>
<thead>
<tr>
<th></th>
<th>N = 73</th>
<th>Gaze Effect</th>
<th>Hand Tuning</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHT</td>
<td>33 (45)</td>
<td>6 (8)</td>
<td></td>
</tr>
<tr>
<td>CUE</td>
<td>20 (27)</td>
<td>50 (68)</td>
<td></td>
</tr>
<tr>
<td>MEM</td>
<td>37 (51)</td>
<td>69 (95)</td>
<td></td>
</tr>
<tr>
<td>RTMT</td>
<td>44 (60)</td>
<td>71 (97)</td>
<td></td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate percentage. ANOVA, $P < 0.05$; bootstrap, $P < 0.01$.

### Table 2. Planar regression analyses for both the gaze and hand regressions

<table>
<thead>
<tr>
<th></th>
<th>Median $R^2$</th>
<th>$R^2 &gt; 0.2$</th>
<th>Median slope, Hz°</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHT</td>
<td>0.07</td>
<td>11 (15)</td>
<td>0.18</td>
</tr>
<tr>
<td>CUE</td>
<td>0.06</td>
<td>7 (10)</td>
<td>0.16</td>
</tr>
<tr>
<td>MEM</td>
<td>0.04</td>
<td>4 (5)</td>
<td>0.16</td>
</tr>
<tr>
<td>RTMT</td>
<td>0.09</td>
<td>15 (21)</td>
<td>0.46</td>
</tr>
<tr>
<td>MEM (no target fix)*</td>
<td>0.07</td>
<td>7 (10)</td>
<td>0.16</td>
</tr>
<tr>
<td>MEM (PD + adjacent)†</td>
<td>0.07</td>
<td>6 (10)</td>
<td>0.20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Median $R^2$</th>
<th>$R^2 &gt; 0.2$</th>
<th>Median slope, Hz°</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHT</td>
<td>0.01</td>
<td>0 (0)</td>
<td>0.10</td>
</tr>
<tr>
<td>CUE</td>
<td>0.08</td>
<td>16 (22)</td>
<td>0.32</td>
</tr>
<tr>
<td>MEM</td>
<td>0.15</td>
<td>36 (49)</td>
<td>0.47</td>
</tr>
<tr>
<td>RTMT</td>
<td>0.24</td>
<td>41 (56)</td>
<td>0.65</td>
</tr>
<tr>
<td>MEM (no target fix)*</td>
<td>0.17</td>
<td>34 (47)</td>
<td>0.48</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages. N = 73, for all but the last row. * Fixations within 6° of intended movement target were excluded from this analysis. † For this analysis, 62 cells were used and the regression was performed using data only from trials in which the target of movement was toward the cell’s PD or toward one of the adjacent targets.
4A is significantly below the diagonal identity line (paired t-test, $P < 0.01$).

Figure 4B shows the results of the second analysis comparing arm- versus gaze-related coordinates. This analysis exploited the monkey’s idiosyncratic tendency to make frequent spontaneous fixations toward a location $18^\circ$ to the left of the center, approximately twice the distance from the center to the leftmost target (see diagram in Fig. 4B). We compared activity of 38 cells whose PD was oriented toward the left, during three types of fixation epochs: A) while the monkey was looking toward the center and planning a movement to the right target; B) looking to the center and planning a movement to the left target; C) looking $18^\circ$ to the left of center while planning a movement to the left target. In a gaze-centered coordinate framework, conditions A and C are identical, and cells tuned to the left should show similar activities in both conditions, and lower than activity in condition B. Conversely, in arm-related coordinates, conditions B and C are identical, and left-tuned cells should show similar activities in both, and higher than in condition A. Histograms of activities from 38 left-tuned PMd cells support the arm-related coding hypothesis ($A < C$, paired $t$-test, $P < 0.01$; number of fixations in A = 558, B = 564, C = 90), and similar results were obtained with cell-by-cell analyses (not shown). Although there is evidence of a trend for activities in C to be lower than in B, reflecting a possible gaze-related modulation, this was not statistically significant.

Note that the analyses in Fig. 4, A and B do not imply that PMd reach-related activity is coded in hand-centered extrinsic coordinates as opposed to other possible coding systems, such as shoulder-related or joint angle-based frameworks. We used “target-re-start” coordinates here only to demonstrate that instructed-delay period activity is more strongly related to reaching movement variables expressed in an arbitrarily chosen arm-related coordinate system than in one centered on the current location of gaze fixation.

Effect of gaze on PMd tuning functions

Figure 4C shows the distribution of PD shifts between tuning functions computed during central versus leftward fixations. The median PD shift was only $1.5^\circ$. For cells where enough data were collected to generate statistically significant ($P < 0.01$) tuning functions during both central and leftward fixations ($n = 18$), the median PD shift was only $-1.1^\circ$. The mean of this distribution is not statistically different from zero ($t$-test, $P > 0.5$). Thus in this small sample of cells, there was no evidence of a systematic counterclockwise rotation of cell tuning functions when the monkey happened to look to its left, compared with those tuning functions while the monkey looked toward the center.
common as in PMd, the strength of the effect was often greater.
Two example cells are shown in Fig. 2, C and D. The cell in
Fig. 2C exhibited a very strong planar effect of gaze, during
both CHT ($R^2 = 0.72$) and MEM ($R^2 = 0.74$). Several cells
exhibited hemifield or even more spatially localized effects
(Fig. 2D) or target fixation effects (not shown), indicating that
a planar function was not the best regression model for a
number of these cells. Nevertheless, in contrast to PMd, the
gaze-direction $R^2$ values during the delay period were larger
for most parietal cells than the target-re-start $R^2$ values, as
shown in Fig. 3D.

In agreement with previous studies (Batista et al. 1999), cells
in medial parietal cortex appeared to code the intended move-
gment in a gaze-centered coordinate system. As shown in Fig.
4A, the planar regressions of parietal activities during MEM
were significantly better when intended final hand position was
expressed relative to gaze than relative to the hand starting
position (paired $t$-test comparing $R^2$ values, $P < 0.01$). Fur-
thermore, although only 6 cells were studied whose PDs during
MEM were oriented to the left, the histograms of their activities
during the three fixation conditions shown in Fig. 4B
support the gaze-centered hypothesis ($C < B$, $P < 0.01$;
number of fixations in A = 84, B = 87, C = 18).

**DISCUSSION**

The existence of gaze-related discharge modulation in PMd
during experimentally controlled fixation (Boussaoud et al.
1998; Jouffrais and Boussaoud 1999) raises several questions.
Is such modulation present during the brief fixations which
classifiﬁc natural unconstrained behavior? If so, then how
does it compare to the modulation of cell discharge by arm
movement-related variables? Are reach plans in PMd ex-
pressed in gaze-centered or arm-related coordinates? And fi-
ally, might gaze-related modulation have confounded many
previous studies of PMd activity in which oculomotor behavior
was not controlled or monitored?

In this preliminary report, we found that gaze-related modu-
lization is present in PMd even during natural unconstrained
oculomotor behavior. However, we also found that the strength
of this modulation is generally low, and this conclusion was
consistent across all the analyses we performed. Second, PMd
activity is much more strongly affected by arm movement-
related variables than by gaze direction-related variables.
Third, these arm movement variables appear to be coded in a
coordinate framework related to the arm rather than in gaze-
centered coordinates. In contrast, neural activity in medial
parietal cortex is more strongly modulated by gaze direction,
and arm movement variables appear to be coded in an gaze-
centered coordinate frame, as reported previously during con-
strained fixation tasks (Batista et al. 1999).

The stronger relation of PMd activity to arm-related than
gaze-related variables might reﬂect methodological factors.
For instance, the coordinate framework for the planning of
movements might differ between a behavioral context of con-
tinually shifting free gaze and one of lengthy fixation in which
the direction of gaze can provide a stable reference point for
planning. Batista et al. (1999) reported that medial parietal
cells re-computed reach target location when monkeys made an
intervening saccade to a different location. However, the in-
tervening saccade was experimentally imposed in their para-

**Gaze-related modulation in medial superior parietal cortex**

In addition, we investigated gaze-related modulation in 35
cells recorded in medial parietal cortex. These parietal results
are presented here for comparison to the PMd data, but their
complete analysis is beyond the scope of this report. While the
incidence of signiﬁcant gaze-related modulation among these
cells (54% during MEM, ANOVA $P < 0.05$) was about as

![FIG. 4. A: scatter-plots comparing the $R^2$ values of regressions of cell activity during MEM against final hand position relative to starting positon (target-re-start) vs. the intended position in gaze-centered coordinates (target-re-gaze). Most of the premotor cells lie below the identity line (paired $t$-test, $P < 0.01$), implying arm-related coordinates, while most of the parietal cells lie above it ($P < 0.01$), implying a gaze-centered representation. B: a second method of testing the hypotheses of arm- and gaze-related coding of intended final hand position. The diagram illustrates 3 kinds of fixation epochs which occur during MEM: A) while the monkey is looking toward the center and planning a movement to the right target; B) looking to the center and planning a movement to the left target; C) looking $18^\circ$ off to the left while planning a movement to the left target. For cells whose PDs lie in the left half-circle, the hypothesis of target-re-start coding predicts activity in both B and C to be greater than in A, while the hypothesis of target-re-gaze coding predicts activity in both A and C to be less than in B. Bar graphs show the data for PMd and parietal cells. C: differences in the PD computed based on PMd cell discharge while the monkey ﬁxated $18^\circ$ to the left compared with the PD collected while the monkey ﬁxated the center. Solid wedges indicate cells where enough data were collected to generate statistically signiﬁcant ($P < 0.01$) tuning functions during both central and peripheral ﬁxations.](http://jn.physiology.org/Downloadedfrom)
dig, not spontaneously made, and the monkey had to fixate that location for 600 ms. The question of context dependence of gaze-related modulations in free gaze versus experimentally controlled gaze requires further study.

It is also possible that the brief natural fixations in this study did not permit sufficient time for the gaze effect to be fully expressed. The temporal dynamics of the gaze-related modulation in PMd are not known. Nevertheless, the gaze-related modulation observed in the free-fixation condition of the present study appears to be quantitatively similar to that reported for PMd under conditions of lengthy controlled fixation. In particular, the distribution of the slopes of planar regressions of PMd activity against gaze direction (Fig. 3A) is very similar to the distribution of slopes reported by Boussaoud et al. (1998) (Fig. 17). Those authors did not report the distribution of $R^2$ values, so we cannot use that measure to compare with our results.

In comparison with PMd, gaze-related modulation in superior parietal cortex was more striking. We found several cells with clear planar gain fields (Fig. 2C) as well as hemifield or more spatially localized effects (Fig. 2D). This verifies that an analysis of cell activity against gaze direction sampled during voluntary free fixations is capable of identifying gaze effects in the appropriate cell populations, and that the low strength of gaze-related modulation observed in PMd cannot be due exclusively to methodological limitations, the temporal dynamics of gaze modulation, or context-dependent changes in coordinate systems.

Furthermore, both analyses aimed at comparing target-restart coding versus target-re-gaze coding suggested that intended movements are represented in an arm-related coordinate frame in PMd (Fig. 4, A and B). In contrast, both analyses suggest that movement coding in medial parietal cortex is better captured in a gaze-centered frame. Again, the term “target-re-start” does not necessarily imply coding of movement in extrinsic hand-centered coordinates.

The modest gaze-related modulation in PMd, as well as the absence of gaze-related PD shifts (Fig. 4C), suggests that gaze direction should not have significantly confounded the results of previous studies of arm movement-related cell discharge in PMd in which oculomotor behavior was not controlled or monitored. For instance, we investigated the possibility that the PD shifts observed by Caminiti et al. (1991) between different parts of space were due to a systematic change in the monkey’s gaze direction. Caminiti et al. reported PD shifts which were similar to the change in the angle between the monkey’s shoulder and the center of each workspace. For example, between the left and the central workspaces, whose centers were separated by 21.8°, the median PD shift was 19°. Thus if those PD shifts were caused only by a change of gaze, then similar shifts should be observed in our data between tuning functions collected during central versus leftward fixations without a change in starting arm posture. However, we found no evidence of such shifts in our data when gaze changed but the arm position did not. Conversely, Sergio and Kalaska (1997) found significant systematic PD shifts in an isometric task when the position of the hand was moved in the workspace but gaze direction (oriented toward a stationary target display) was not. Thus a shift of PDs in different parts of the workspace clearly appears to be dependent on the arm configuration, not the direction of gaze.

In conclusion, the gaze-direction effect in PMd is sufficiently rapid that it can significantly modulate the reach-related activity of cells during the brief fixations that are characteristic of natural oculomotor behavior. Nevertheless, these modulations are typically more modest than the reach-related activity of the same cells. It is not likely that such effects could have seriously confounded the results of many previous studies of arm movement-related PMd activity in which oculomotor behavior was not controlled or monitored. Nevertheless, these results do not mean that gaze modulation effects in PMd can be ignored completely; they must be accounted for in the appropriate experimental situations. In contrast to PMd, gaze-related modulation of reach-related medial parietal cells is stronger, and these cells appear to code reach plans in gaze-centered coordinates during both unconstrained and constrained fixation conditions (this study, Batista et al. 1999).

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