

RESEARCH NOTE

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Neuronal activity related to eye-hand coordination in the primate premotor cortex

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Abstract To test the functional implications of gaze signals that we previously reported in the dorsal premotor cortex (PMd), we trained two rhesus monkeys to point to visual targets presented on a touch screen while controlling their gaze orientation. Each monkey had to perform four different tasks. To initiate a trial, the monkey had to put his hand on a starting position at the center of the touch screen and fixate a fixation point. In one task, the animal had to make a reaching movement to a peripheral target randomly presented at one of eight possible locations on a circle while maintaining fixation at the center of this virtual circle (central fixation + reaching). In the second task, the monkey maintained fixation at the location of the upcoming peripheral target and, later, reached to that location. After a delay, the target was turned on and the monkey made a reaching arm movement (target fixation + reaching). In the third task, the monkey made a saccade to the target without any arm movement (saccade). Finally, in the fourth task, the monkey first made a saccade to the target, then reached to it after a delay (saccade + reaching). This design allowed us to examine the contribution of the oculomotor context to arm-related neuronal activity in PMd. We analyzed the effects of the task type on neuronal activity and found that many cells showed a task effect during the signal (26/60; 43%), set (16/49; 33%) and/or movement (15/54; 28%) epochs, depending on the oculomotor history. These findings, together with previously published data, suggest that PMd codes limb-movement direction in a gaze-dependent manner and may, thus, play an important role in the brain mechanisms of eye-hand coordination during visually guided reaching.

Key words Premotor cortex · Eye-hand coordination · Single-unit recording · Monkey · Arm movement · Context

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Introduction

It is traditionally accepted that the dorsal premotor cortex (PMd) is involved in limb-movement preparation, namely movements guided by sensory information. Several laboratories have been investigating whether PMd's neuronal activity reflects movement attributes, such as direction, the visuo-spatial properties of visual targets that guide the movement, or even spatial attention (Boussaoud et al. 1996; Caminiti et al. 1996; Wise et al. 1997). It appeared from these studies that, in general, the discharge pattern of PMd cells is primarily correlated with extrinsic parameters of limb movement, although it may be modulated by a variety of task factors. Recently, we have shown that gaze angle strongly modulates the cell properties in PMd (Boussaoud et al. 1998), suggesting, among other possible functional implications, that PMd may play a role in the brain mechanisms for eye-hand coordination. We made the prediction that, if gaze signals are used to build limb motor commands, limb-related activity should depend on whether or not the monkey made a saccade to the target prior to the reaching movement. To examine this possibility, we analyzed the activity of PMd neurons under four tasks that dissociate the relative contributions of gaze shift and limb movement. The findings show that the discharge pattern of many cells depends on whether the monkey performed a limb movement after a saccade to the target, a limb movement while fixating, or just a saccade without any overt limb movement.

Materials and methods

Behavioral paradigms

Two male rhesus monkeys (*Macaca mulatta*), 5 and 8 kg, were used in the present study. They were seated in a primate chair with the head firmly fixed and were trained to point to visual targets presented on a touch screen located at arm's reach. As the monkeys were free to use their preferred hand, one monkey pointed with the left forelimb, the other monkey used the right forelimb.

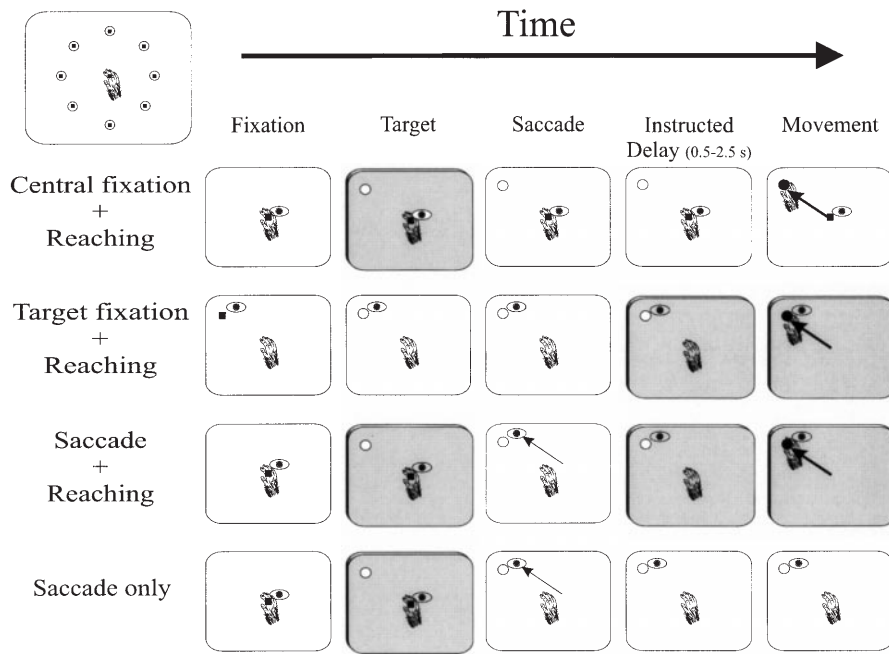


Fig. 1 Schematic representation of the experimental design. Four examples of trials illustrating the different tasks. The *large rectangle* represents the touch screen, the *small filled square* the fixation point, and the *circle* the target for limb movement (*open target* is bright, *filled target* is dim). The *arrows* indicate the direction of the limb intended movement. The *upper left drawing* shows the location of the eight targets and the nine fixation points used in the tasks. In the *left column*, the monkey's hand was at the initial starting position, and gaze was on the fixation point. A target was presented (*second column*), and the monkey saccaded to it (*thin arrow*) or kept fixating (*third column*). The *fourth column* represents a delay period, during which the monkey prepared to move the limb to the target (except for the "saccade-only" task). When the target dimmed (*right column*), the monkey executed the reaching movement. The *shading* indicates task epochs where behavioral context differed, but eye, head, and target position were identical. See text for more details

Eye position was monitored using a scleral search coil. All surgical and experimental procedures were in accordance with the Guiding Principles in the Care and Use of Laboratory Animals of the National Institutes of Health and the European Community's guidelines for animal protection and use for experimentation.

The behavioral paradigm is schematically represented in Fig. 1. Each monkey performed four different tasks, all of which began when the monkey placed its hand on a central position on the touch screen and oriented its gaze to a fixation point ($0.3 \times 0.3^\circ$). Then, a target (a white circle, 2° diameter) was presented at a randomly selected location among eight potential ones equidistant from the hand starting position (Fig. 1, top left). The offset of the fixation point instructed the monkey to make a saccade to the target, and a dimming of the target instructed the animal to reach to that target with the hand.

In the "central fixation + reaching task" (CR), the target appeared while the animal was fixating at the center. Then, the target dimmed and the monkey reached to the target without moving its gaze. In the "target fixation + reaching task" (TR), the fixation point was presented at one of the eight potential target locations. While the animal was fixating, the target appeared at the fixation location. After a delay, the target dimmed and the monkey made a reaching movement. In the "saccade + reaching task" (SR), the target appeared at a given location while the animal was fixating

the central fixation point, as in the CR task. After an initial delay, the fixation point went off and the monkey made a saccade to the target. Then, after a second delay, the target dimmed and the monkey made a reaching movement. Finally, in the "saccade-only task" (S), the monkey made a saccade from the central fixation point to the target and waited to receive a reward. Electromyographic (EMG) recordings confirmed that there was no overt arm movement in this task.

In all four tasks, the delay period corresponding to the preparation of a limb movement (i.e., between target onset and its dimming in the CR and TR tasks, and between the end of the saccade and the dimming in the SR task) was varied pseudorandomly between 0.5 and 2.5 s. In the CR, TR, and SR conditions, the monkey had a maximum delay of 1 s after the go signal to lift its hand from the starting position and contact the target's location, while maintaining fixation.

Neural recordings and data analysis

The four tasks were presented in blocks and the monkey had no cue between consecutive blocks that would indicate the task to be performed. First, to ensure that the cells were tested in all four tasks, four targets located at the corners of a virtual square centered on the hand position were used. After three correct trials were performed for each target and for each task ($4 \text{ tasks} \times 4 \text{ targets} \times 3 \text{ trials} = 48 \text{ trials}$), the remaining four targets were presented and three trials per task were performed (another 48 trials). The same sequence of blocks was run a second time in order to collect data during the performance of six correct trials per target location in each task. While the monkey performed the tasks, conventional methods of extracellular recordings were used to collect action potentials of single neurons in relation with the behavioral events (Boussaoud et al. 1998).

A paired *t*-test was used to compare the mean discharge rate during selected trial epochs with the activity during a reference period. The three main epochs considered for analysis of neuronal activity were the short period following target onset (signal-related, 75 ms after target appearance, and during 125 ms), the delay period (set-related, 300 ms before the go signal), and the response time (movement-related, from the go signal to the end of the movement). The reference period activity was recorded during 300 ms at the beginning of each trial, 50 ms after the monkey put its hand on the starting position, and 150 ms before onset of the fixation point.

Fig. 2 Surface plot of the recording sites. At each site, the number of task-related cells is indicated by the size of the dot, following the scale shown in the figure. *Ce* Central sulcus, *iAr* and *sAr* inferior and superior branches of the arcuate sulcus, respectively, *M1* primary motor cortex *Pr* principal sulcus, *PMd*, dorsal premotor cortex

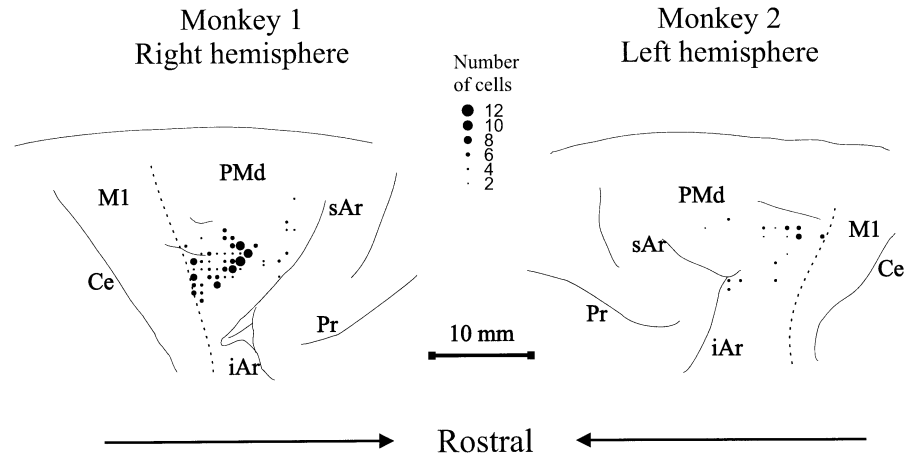


Table 1 Summary of neuronal categories. *First column* Task periods analyzed (see text). *Second column* The “task-related” column shows the number of cells whose discharge rate presented a difference between the selected task period (signal, set, or movement epochs) and the reference period (*t*-test, $P < 0.05$). *Third column* Cells whose activity did not significantly vary in time (*t*-test, $P < 0.05$). Those with significant variation were excluded from the analysis. *Right column* Numbers (and percentages) of neurons whose discharge rate varied in relation to the oculomotor context

Task period	Task-related	Data base	Effect of oculomotor context
Signal	75	60	26/60 (43.3%)
Set	70	49	16/49 (32.7%)
Movement	63	54	15/54 (27.8%)

Because of the long time period separating the recording of the first and the last conditions, we tested the cells in blocks of trials, as described above, in order to minimize the effects due to changes of activity with time. In addition, we made recordings during six correct trials for each target position in the CR task at the beginning and at the end of the session to be certain that systematic temporal changes did not influence the collection of spike data. The task-related neurons presenting a difference in activity [two-factor analysis of variance (ANOVA): time \times direction; $P < 0.05$] due to time of recording were excluded from the present analysis.

We then analyzed different periods that were identical across the tasks of visual stimuli as well as in eye and hand position, but which differed only in terms of oculomotor context. In the CR, SR, and S tasks, the target appeared while the monkey was fixating at the center of the screen (see Fig. 1, shaded drawings in the “target” column). We used a two-factor ANOVA (SYSTAT) to test whether the location of the target (i.e., movement direction) or the task type significantly ($P < 0.05$) affected the mean discharge rate during the signal-related epoch. The same analysis was made to compare the set- and movement-related activity during the TR and SR tasks (see Fig. 1, shaded drawings in the “delay” and “movement” columns, respectively). In both tasks, the monkey’s gaze was on the target of the upcoming limb movement.

Results

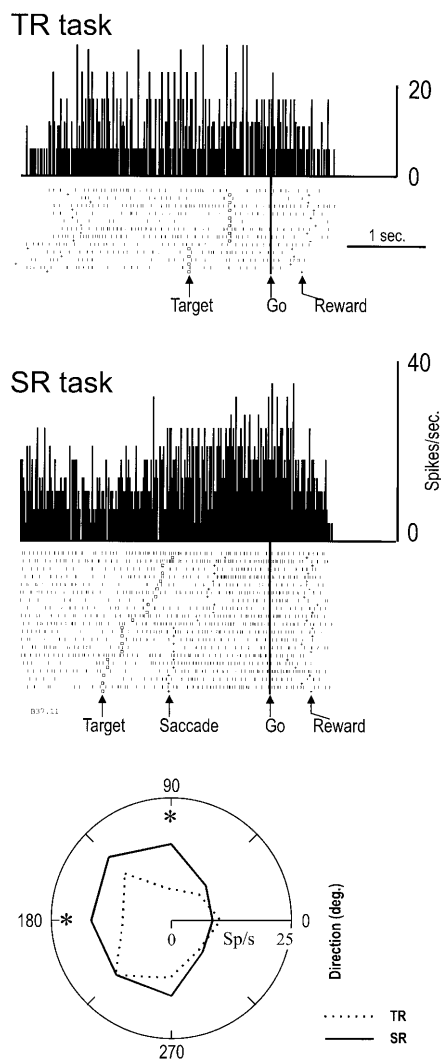
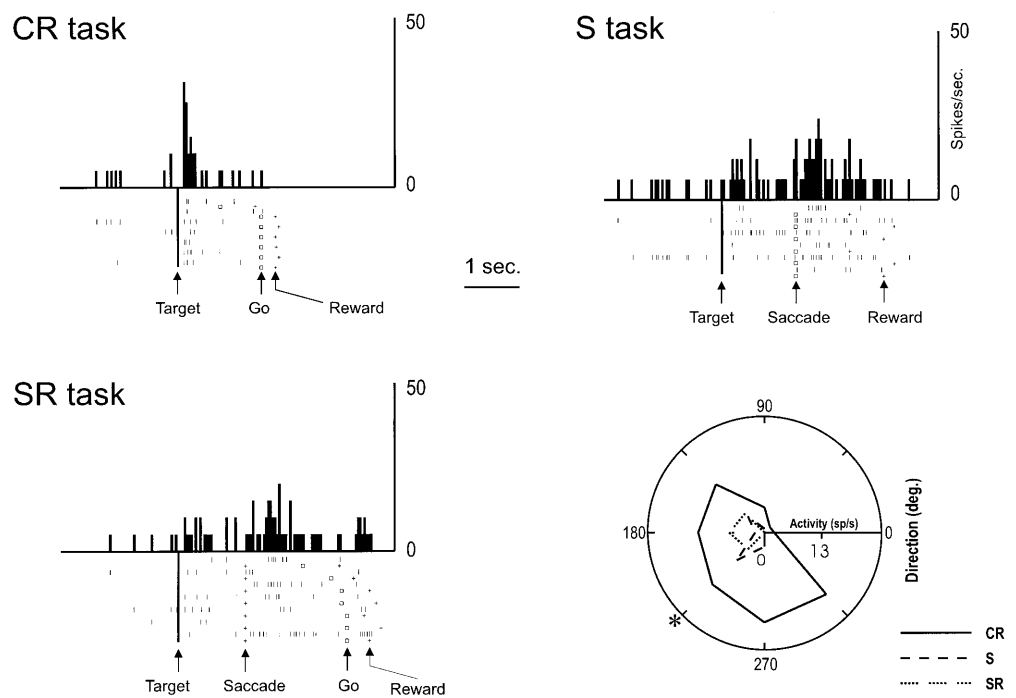
We recorded the activity of 100 PMd neurons in two monkeys, among which 83 neurons were related to at least one task event (exhibiting signal-, set-, and/or

movement-related activity). Figure 2 shows surface plots of the recordings. Among this neuronal sample, 60 displayed phasic activity following target onset (signal-related activity), 49 were active during the instructed delay period (set-related activity), and 54 were active during the response time (movement-related activity; see Table 1).

The ANOVA showed that the neuronal discharge of a substantial proportion of cells was significantly different ($P < 0.05$), depending on the task-behavioral oculomotor context in which limb movements were performed by the monkey. The proportion of cells with such a task dependency varied across the three epochs analyzed (Table 1). This proportion was highest for signal-related activity (43% of cells), lowest for movement-related activity (28%), and in-between for set-related activity (33%).

Figure 3 shows an example of a cell whose signal-related activity was task-context specific. In this cell, target onset was followed by a vigorous phasic discharge in the CR task. However, when the same target was presented in the SR or S tasks, the discharge was almost absent after target onset, although the target was presented at the same location as in the CR task. The polar plot in Fig. 3 depicts the signal-related activity for all target locations tested. It appears that the cell was active and broadly tuned in the CR task, but quite silent in the SR and S tasks. Figure 4 shows another cell whose set-related activity was different, depending on the task. The raster displays illustrate the activity patterns for two directions of movement (90° and 180° pooled together), and the polar plot shows the mean set-related activity of the cell measured during either the TR or SR task for the eight movement directions. This neuron was broadly tuned, independently of the task, but the mean discharge rate was higher when the monkey prepared a reach following a saccade (SR task) than when he prepared the same movement while maintaining target fixation (TR task). In this cell, the modulation of the discharge was especially observed for those directions with the highest discharge rate, that is, in the preferred direction.

Fig. 3 Task effect on signal-related activity. Raster displays and histograms of the discharge frequency (bin width 21 ms) of a dorsal premotor cortex cell for a target presented at 225° . The rasters are aligned on target onset. The monkey made a limb movement after the go signal while maintaining central fixation (*CR task*), a saccade followed by a reaching movement (*SR task*), or only a saccade with no reaching movement (*S task*). *Bottom right* Polar plot of the signal-related activity of the same cell. The *star* indicates the target angle used to construct the raster displays and histograms



Discussion

In this report, we briefly describe a population of PMd neurons, the activity of which reflects the behavioral oculomotor context in which limb movements were performed. Although we herewith confirm that the activity of PMd neurons is spatially tuned for target location and/or the direction of the planned movement (Caminiti et al. 1991; Boussaoud and Wise 1993a; di Pellegrino and Wise 1993; Crammond and Kalaska 1994; Mason et al. 1998), the significant difference we describe in the mean discharge rate of the cells across the tasks cannot be accounted for by these two factors. Indeed, during the signal-related activity (compared in the CR, SR, and S tasks), as well as the set- or movement-related activity (compared in the TR and SR tasks), gaze and hand positions as well as the fixation point and target locations are identical. In addition, we can reasonably exclude a difference in the attentional demand. For example, spatial attention in both TR and SR tasks was presumably on the fixated target. A more likely explanation of the observed modulation of the discharge relates to the oculomotor context within which limb movements were performed toward visual targets, that is, the so-called eye-hand coordination. In the CR task, target presentation was followed by a limb movement, whereas in the SR and S tasks the same visuo-spatial event was followed by an eye movement. Therefore, the signal-related activity that appeared af-

Fig. 4 Task effect on set-related activity. Raster displays and polar plot of the activity of a dorsal premotor cortex cell. Same conventions as in Fig. 3, except that the trials in *TR* ("target fixation + reaching", see Materials and methods) and *SR tasks* are aligned on the go signal. Bin width 16 ms. In both conditions (TR and SR tasks), the trials are pooled for target presentation at 90 and 180° . *Bottom* Polar plot of the mean discharge rate during the delay period for the same cell

ter a given target seems to reflect the motor significance of the target. These findings resemble those described in previous studies (Boussaoud and Wise 1993a, 1993b; di Pellegrino and Wise 1993), showing that signal-related activity depends on the direction of the upcoming limb movement. Here, movement dependency of neuronal activity was extended to different motor domains, such as oculomotor versus skeletomotor behavior.

Eye-hand coordination has been extensively described from the psychophysical perspective (Biguer et al. 1982; see Abrams 1992 for a review). In this report, we present neurophysiological evidence for the convergence of eye- and limb-related signals on single PMd cells. Other studies have reported the presence of arm movement and gaze signals in the parietal area 7 m (Ferraina et al. 1997), the supplementary eye field (SEF; Mushiaki et al. 1996), and in the superior colliculus (Werner 1993; Werner et al. 1997). These areas, together with PMd, may form a network for visuomotor transformation in eye-hand coordination. Indeed, although the source of interactions between the oculomotor and skeletomotor systems is not, at first glance, apparent in the literature, there are several possible pathways for mediating such interactions. One obvious possibility is within the parieto-premotor networks, as medial parietal areas (7 m, PO, MIP) strongly project to PMd (Tanné et al. 1995; Johnson et al. 1996) and have reciprocal connections with areas LIP and 7a of the inferior parietal lobule (Cavada and Goldman-Rakic 1989a, 1989b; Andersen et al. 1990). The latter areas are known to play a crucial role in oculomotor behavior (see Andersen et al. 1997 for a review). In addition, LIP and 7a have direct projections to PMd (Tanné et al. 1995). Although these projections are quantitatively less dense than those arising from the medial parietal cortex, they may nevertheless play an important role in transmitting oculomotor signals to PMd. Finally, PMd has connections with the supplementary eye field (Tanné et al., personal communication) and projects to the superior colliculus (Fries 1985). These, and possibly other cortical and sub-cortical pathways, may mediate interactions between eye and limb motor centers and may subserve eye-hand coordination.

The question remains as to how the oculomotor behavior might affect limb movement preparation. One possibility might be that PMd receives an efference copy signal from the oculomotor system. In this view, the efference copy is reflected in the SR task, but not in the CR and TR tasks, as no saccade was made prior to the limb movement. Such a hypothesis remains to be tested.

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