Neuronal Activity in the Ventral Part of Premotor Cortex During Target-Reach Movement is Modulated by Direction of Gaze

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INTRODUCTION

The premotor cortex (PM) of primates has been implicated in sensorial guidance of arm movements (Godschalk et al. 1985; Kurata 1994; Wise 1985). It is well established that neurons in the primate PM exhibit activity changes during execution of movements, as well as during motor preparation, and in response to sensory signals (Evarts 1981; Godschalk et al. 1985; Passingham 1985; Wise 1985). The lateral part of PM is now subdivided into its ventral and dorsal parts (PMv and PMd, respectively). The movement-related activity of both PMv and PMd neurons has a number of properties in common with that observed in the primary motor cortex (MI) (Godschalk et al. 1981; Kalaska and Crammond 1992; Weinrich et al. 1984). During reaching to visual targets, neurons in the PMd and MI appeared to be similarly related to the direction of arm movements in space (Caminiti et al. 1991; Georgopoulos et al. 1982). On the other hand, some differences in activity properties (such as relations to motor parameters or sensory responses to visual signals) have been found among neurons in the PMv and MI (Gentilucci et al. 1988; Kubota and Hamada 1978; Kurata and Tanji 1986). A question then arises as to whether the two areas are involved similarly or differently in visual guidance of arm-reaching movements. In this series of experiments, we chose to study the neuronal activity in the PMv rather than PMd, because a previous study of temporal inactivation of PMv and PMd revealed that the PMv is more critically involved in visual guidance of arm-reaching movements than the PMd (Kurata and Hoffman 1994). Soechting and colleagues (Flanders et al. 1992; Soechting and Flanders 1992) put forth a hypothesis that, in visually guided arm-reaching tasks, the neural representation of target parameters is first transformed from a retinocentric to a shoulder-centered representation. In later stages the transformation is made from kinematic to dynamic parameters of arm movements. It is of interest to know the extent to which the neuronal activity in the PMv and MI is involved in the early or late stage of the transformation (Jannarder 1994; Kalaska and Crammond 1992). Relevant to this issue are recent reports that responses to visual signals of the PMv and motor-set-related activity of the PMd neurons were modulated by the direction of gaze (Boussaoud 1995; Boussaoud et al. 1993). The visual receptive field was also modulated by the position of arm (Graziano et al. 1994). In these reports, however, the neuronal activity during execution of movements was not examined. Moreover, motor tasks employed in previous reports did not particularly require animals to use visual signals for spatial guidance of arm movements. Thus, in the present study, the effect of the direction of gaze on PMv and MI neurons was studied during a visually cued arm-reaching task while the subject was required to maintain gaze at different fixation points. In this report, we focus on the movement-related activity in the PMv and we show that the movement-related activity of a group of PMv neurons, but not of MI neurons, is influenced by the direction of gaze.

METHODS

We recorded neuronal activity in the PMv and the MI of an adult monkey (Macaca fuscata) during performance of a visually cued arm-reaching task. The animal was cared for in accordance with the Guiding Principles in the Care and Use of Laboratory Animals of the National Institutes of Health. The animal sat in a primate chair with the head restrained, facing a panel equipped with two fixation targets and seven arm-reaching targets. We placed the two fixation targets, light-emitting diodes (LEDs) 0.5° diam, 20° apart, at the monkey’s eye level. We also placed four reaching targets (circular button 28 mm diam, back-illuminated with LED) at the top, left, right, and bottom of each fixation target at a distance of 10° from either the right or left fixation target. The central reach target was therefore placed straight ahead, 10° right from the left fixation target and 10° left from the right fixation target (Fig. 1A).
When the animal placed the right hand on a hold plate in front of the chair, one of the two fixation targets was turned on, at which the monkey was required to fixate. If the fixation was maintained for 800 ms (hold period) within a 2° window, a reaching target, randomly selected from the four surrounding the fixation target, was illuminated for 300 ms, serving as both an instruction and a target for a subsequent, forthcoming arm reach. The monkey was required to keep fixating on the fixation target for a variable period of 1.5–3.5 s without shifting the gaze from the fixation window, and then to be prepared to reach to the illuminated reach target. If the animal accomplished the fixation during the delay period, the fixation point was dimmed, serving as a GO signal to initiate the arm reach to the instructed target. Reward was delivered when the animal captured the target within 800 ms after the GO signal while maintaining the gaze at the fixation target. The movement onset was defined as the time when the animal released the hold key before reaching to the target. We used conventional electrophysiological techniques for single-cell recording in behaving monkeys (Mushiake et al. 1991). The boundary between the MI and PM was drawn according to the criteria previously proposed (Kurata and Tanji 1986; Weinrich et al. 1984). We recorded eye movements with the use of a scleral search coil (Judge et al. 1980). Electromyographic recordings were made from muscles in the digits, wrist, elbow, shoulder, neck, thigh, and also from paravertebral muscles. In this paper we studied neurons exhibiting movement-related activity, defined as changes in activity preceding and time-locked with the movement onset (Weinrich et al. 1982). Other types of neurons such as delay-related or visual-signal-related neurons were found but not included in this paper. To see whether the activity change was time-locked with the movement onset or GO signal, we made a statistical analysis. We compared variations of the interval between the GO signal and the onset of neuronal activity changes with variations of the time interval between the onset of activity changes and the movement onset. The variations were calculated as deviations of intervals in individual trials from a mean interval value obtained from a data set. If the variations of the latter (neuronal movement-preceding time) were significantly smaller ($P < 0.05$, F-test) than the former (neuronal response time), we called these activities “movement-related” and used them for further analysis. All of “movement-related neurons” were broadly tuned to direction of movement. There was no difference in the degree of direction selectivity of MI and PMv neurons. After completion of neuronal recording, the monkey was killed with an overdose of pentobarbital sodium (50 mg/kg) and perfused with saline followed by 8% Formalin. Fifty-micrometer coronal sections of the brain were made with a freezing microtome and stained with cresyl violet. Electrode tracks were reconstructed with reference to microlesions made by direct currents through Elgiloy-alloy electrodes.

**RESULTS**

Before analyzing neuronal data, we analyzed activities recorded from limb and axial muscles. In Fig. 1B, we show typical examples of forelimb muscle activity before and after the onset of the reaching movement to the central target. The activity shown in Fig. 1B, left and right, was recorded when the animal reached to the same central target while gazing at the left and right fixation targets, respectively. As shown in the figure, the movement-related activities in the three muscles are similar, uninfluenced by the direction of gaze. In relation to the reaching movements to the other six targets, no statistical differences were found between muscle activities during left- and right-target fixation. We further found that the activity of any muscles (including neck and trunk muscles) in relation to execution of the reaching task was not different regardless of whether the animal was gazing at the left or right fixation target.
We next analyzed the activity of 200 neurons recorded in the PMv. Their recording sites, shown in Fig. 2A, were caudal to the arcuate sulcus, lateral to its spur, and rostral to the MI. What was remarkable in 41% of the PMv neurons was that their movement-related activity was different depending on whether the animal was gazing at the left or right fixation point during reaching. A representative example of such a case is shown in Fig. 2B, where the neuron is active when the animal reached to the central target while gazing at the right fixation point (top). The same neuron, however, was not active when the animal reached to the same target while gazing at the left fixation point (bottom). In these 81 PMv neurons, statistical analysis of the movement-related activity revealed significant differences ($P < 0.01$, t-test, made on the data obtained in individual trials) under the two gaze conditions. In contrast, a vast majority of neurons recorded in the MI did not show such influence of the direction of gaze. As in the example shown in Fig. 2C, 106 of 110 movement-related MI neurons (96%) did not exhibit significant differences in activity regardless of whether the animal was gazing at the left or right fixation point.

What about the movement-related activity in relation to reaching to other reach targets? In Fig. 3, the activity of a PMv neuron during reaching to the seven targets is shown. As apparently displayed in the figure, the movement-related activity is greatest during reaching to the left of the fixation target. The same neuron is modestly active during reaching to the top of the fixation point. Further, the neuron was inactive when the animal reached to either the right or bottom of the fixation point. Thus the magnitude of movement-related activity in this neuron, as in the other 80 PMv neurons showing the gaze effect, was primarily determined by the position of the reaching target relative to the eye-fixation point, and not to the position of the target relative to the animal’s body. In a separate paper in the future, we will deal with detailed quantitative analysis on the extent to which the movement-related activity is correlated with direction of the target either relative to the eye-fixation point or relative to the body. On the other hand, there was no difference in the degree of directional selectivity between neurons showing the gaze effect and neurons showing no gaze effect. It was apparent on inspection of the data that hardly any MI neurons exhibited the movement-related activity that was influenced primarily by the direction of gaze.

**FIG. 2.** A: surface reconstruction of cortical recording sites. Filled and open circles: points of electrode entry into the ventral part of the premotor cortex (PMv) and the primary motor cortex (MI), respectively. Rostral is to left, medial is to top. CS, central sulcus; AS, arcuate sulcus. B: discharge of a representative example of a PMv neuron that exhibited selective movement-related activity during reaching to a central button while the monkey was gazing at the right fixation target, but not while gazing at the left target. Rasters and histograms are aligned on movement onset (arrowheads). Dots: neuronal discharges during 1,500 ms before and after movement onset. Triangles and squares in raster display: onsets of trigger signals and presses of target buttons, respectively. Binwidth = 20 ms. C: typical example of an MI neuron showing similar movement-related activity, regardless of whether animal is gazing at right or left fixation point. Display format same as above.
FIG. 3. Discharges of a PMv neuron during reaching to 4 targets placed around right and left fixation targets. Right: animal is gazing at right fixation point. Left: animal is gazing at left fixation point. Histograms: neuronal discharges during reaching to individual targets (A–D on left, A′–D′ on right). Note that central reaching target button is labeled C (in left-gaze condition) and B′ (in right-gaze condition), but is physically a single target. Histograms are aligned on movement onset (arrowheads).

DISCUSSION

The main finding in this study is that >40% of the movement-related activity in the PMv is modulated by the direction of gaze (or eye position in the orbit) maintained during a target-reaching motor task. Further, the magnitudes of the movement-related activity in these gaze-direction-sensitive neurons appear to be primarily determined by the position of the reaching target relative to the fixation point at which the subject maintains the gaze. In contrast, a vast majority of MI neurons is not influenced by where the subject is gazing, and magnitudes of the movement-related activity appear to be determined by the target position relative to the body (or by the target position in space). These data suggest that the “movement-related activity” in the PMv, so called because of its appearance shortly before the movement onset, may have a component that is different from the movement-related activity in the MI.

There has been a controversy as to whether visual responses in the PMv are modulated by the direction of gaze. One group claimed that the location of visual receptive fields of most PMv neurons was not influenced by the direction of gaze but was coded in the body-centered coordinate system (Fogassi et al. 1992; Gentilucci et al. 1983, 1988). The other group claimed that visual responses of PMv neurons or set-related activity of PMd neurons were influenced by the direction of gaze (Boussaoud et al. 1993; cf. Boussaoud 1995). Still another group further claimed that responses of PMv neurons were based on arm-centered coordinate (Graziano et al. 1994). In the present study, it appears that even the movement-related activity in the PMv is modulated by the direction of gaze. This modulation cannot be explained as neuronal visual responses, because, as mentioned above, the reaching targets were not illuminated during execution of the reaching movements. Further, we focused the present study on movement-related neurons whose onset of activity changes was time-locked to the movement onset rather than

the GO signal. The modulation was not due to eye movements or neck movements, because the eyes were fixated on the target during reaching, and neck muscles did not show any changes in activity.

According to a current view, reaching movements to an object in space require transformation of information at multiple stages (Jeannerod 1988; Kalaska and Crammond 1992). At early stages, information of eye position or gaze direction plays an important role in localizing a visual reaching target in space, whereas at late stages, specification of kinematics or dynamics of movements is a major issue (Flanders et al. 1992; Soechting and Flanders 1989). Our data suggest that >40% of PMv neurons, although active in relation to execution of reaching movements, are deeply influenced by gaze signals. Two possible interpretation seem to explain this type of neuronal activity. One is that these neurons reflect a transitional stage of signal transformation in which target positions in the retinotopic frame of reference and gaze position signals are transformed to signals coding directions of movements in the execution period. Andersen et al. (1993) proposed a view that transformations from retinotopic to head-centered coordinate space occur in the posterior parietal association cortex. According to the model of Andersen et al., the posterior parietal cortex is able to combine retinal and orbital signals to code stimulus location in head-centered space at the neuronal population level. Because the PMv receives inputs from V6 (PO) of the superior parietal lobule (Caminiti et al. 1996), which encodes spatial locations in head-centered coordinates (Galletti et al. 1993), the activity of gaze-sensitive PMv neurons found in the present study may be a reflection of the activity in the parietal cortex (Sakata et al. 1994, 1995). The exact source of gaze signals in the PMv, however, remains to be solved. Further study is necessary to solve this issue. An alternative possibility may be that, in the present motor task, PMv neurons code the direction of arm reach in exocentric coordinates with reference to the fixation point.
On the other hand, in the remaining 60% of PMv neurons, the activity is related to the target in space or direction of arm reach in body-centered coordinate and therefore seems to be involved in later stages of information transformation for the achievement of reaching movements. There are at least two possibilities for obtaining this type of position coding. One is by receiving visual signals of location in body-centered coordinate, and the other is by transforming the retinotopic position signals of the other group of PMv neurons into body-centered coordinates taking the eye position signal into account. These data, combined with findings in recent reports, favor a view that the PMv is able to use information about target objects with reference to multiple coordinate frames.

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