Neurons in the Primate Superior Colliculus Coding for Arm Movements in Gaze-Related Coordinates

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Stuphorn, Veit, Erhard Bauswein, and Klaus-Peter Hoffmann. Neurons in the primate superior colliculus coding for arm movements in gaze-related coordinates. *J. Neurophysiol.* 83: 1283–1299, 2000. In the intermediate and deep layers of the superior colliculus (SC), a well-established oculomotor structure, a substantial population of cells is involved in the control of arm movements. To examine the reference frame of these neurons, we recorded in two rhesus monkeys (*Macaca mulatta*) the discharges of 331 neurons in the SC and the underlying mesencephalic reticular formation (MRF) while monkeys reached to the same target location during different gaze orientations. For 65 reach-related cells with sufficient data and for simultaneously recorded electromyograms (EMGs) of 11 arm muscles, we calculated an ANOVA (factors: target position, gaze angle) and a gaze-dependency (GD) index. EMGs and the activity of many (60%) of the reach-related neurons were not influenced by the target representation on the retina or eye position. We refer to these as "gaze-independent" reach neurons. For 40%, however, the GD fell outside the range of the muscle modulation, and the ANOVA showed a significant influence of gaze. These "gaze-related" reach neurons discharge only when the monkey reaches for targets having specific coordinates in relation to the gaze axis, i.e., for targets in a gaze-related "reach movement field" (RMF). Neuronal activity was not modulated by the specific path of the arm movement, the muscle pattern that is necessary for its realization or the arm that was used for the reach. In each SC we found gaze-related neurons with RMFs both in the contralateral and in the ipsilateral hemifield. The topographical organization of the gaze-related reach neurons in the SC could not be matched with the well-known visual and oculomotor maps. Gaze-related neurons were more modulated in their strength of activity with different directions of arm movements than were gaze-independent reach neurons. Gaze-related reach neurons were recorded at a median depth of 2.03 mm below SC surface in the intermediate layers, where they overlap with saccade-related burst neurons (median depth: 1.55 mm). Most of the gaze-independent reach cells were found in a median depth of 4.01 mm below the SC surface in the deep layers and in the underlying MRF. The gaze-related reach neurons operating in a gaze-centered coordinate system could signal either the desired target position with respect to gaze direction or the motor error between gaze axis and reach target. The gaze-independent reach neurons, possibly operating in a shoulder- or arm-centered reference frame, might carry signals closer to motor output. Together these two types of reach neurons add evidence to our hypothesis that the SC is involved in the sensorimotor transformation for eye-hand coordination in primates.

INTRODUCTION

Primates interact with objects in the external space by using their arms on an every-day basis. These spatially oriented motor acts include gaze shifts with eyes, head, and body as well as reaching with the arm. To do this, the incoming visual information has to be transformed from a retinocentric into an effector-related coordinate system. Both the skeletomotor and the oculomotor networks get their visual input via specific pathways connecting certain parietal and frontal cortical areas subserving the control of the eye (Tian and Lynch 1996), arm (Caminiti et al. 1996) and hand (Murata et al. 1997; Sakata et al. 1995). Each type of effector poses different computational problems and differently assorted types of sensory information are needed to control the movement. During eye movements, the direction of the movement vector and the torque of the eyeball coincide. This relieves the brain from an additional computational step from a kinematic (desired movement) to a dynamic (forces needed to perform the desired movement) command. In the case of arm movements, the brain cannot omit such a step because in this system the relationship between kinematics and dynamics is nontrivial (Hollerbach and Flash 1982). Another difference is the origin of the reference frames for the signals controlling either the oculomotor or the skeletomotor system. Naturally both are aligned to their respective effectors. Consequently the oculomotor system refers to the gaze axis, whereas the skeletomotor system refers to the joints of the arm.

Nevertheless it is of great importance to align the gaze axis and the point in space at which the arm is aiming. The great number of psychophysical studies showing eye-hand interactions is in accordance with this need to integrate the activity of the main effectors into a synergistic pattern (Bekkering et al. 1995; Biguer et al. 1982; Blouin et al. 1996; Goodale et al. 1986; Jeannerod 1988; Prablanc and Martin 1992). For that reason, one should expect to find nodal points in the brain where the oculomotor and skeletomotor networks interact.

The superior colliculus (SC) is known to be a crucial part of the oculomotor system (Schiller et al. 1987; Sparks and Hartwich-Young 1989; Wurtz and Goldberg 1971) and also is involved in the control of head movements (Cowie and Robinson 1994; Freedman and Sparks 1997; Freedman et al. 1996; Guitton 1992; Paré et al. 1994). Besides this gaze-controlling system, the SC contains a population of cells involved in the control of goal-directed arm movements (Werner 1993; Werner et al. 1997a,b). Because the SC contains gaze- and arm-movement-related signals, it might constitute another region in the brain in addition to parietal and frontal cortical areas where the control signals for eye and arm movements can be coordinated (Wise et al. 1997). If this coordination hypothesis is correct, the system controlling one of the effectors (e.g., the arm) should be no longer independent of the state of the

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other (e.g., the gaze). Instead one might expect to find a relationship between the spatial orientation of gaze and the discharge of arm-movement-related cells in the SC.

To test the influence of gaze direction on arm-movement-related activity in the SC, we trained two monkeys to reach to a set of eight targets in two gaze conditions. First, the monkey looked at the target while he reached to it, and second, he fixated a light-emitting diode (LED) away from the target he reached to. With these tasks, we separated gaze and reach and thus were able to show that reach neurons in the SC were related to target location with respect to gaze axis. Preliminary reports of the work have been made previously (Bauswein et al. 1997; Stuphorn et al. 1995)

METHODS

The experiments were conducted on two male rhesus monkeys (*Macaca mulatta*, 8 and 9 kg). The animals were seated comfortably in a primate chair with their heads restrained, facing a tangent screen. The distance between the eyes and the screen was 29 cm for the larger and 28 cm for the smaller monkey. The animals were trained to perform a delayed saccade task and two delayed reach tasks toward light spots of 0.8° diam appearing on the screen. A plastic cylinder around the upper and lower arm loosely restrained the nonworking arm in the reach tasks. All procedures were approved by a local ethical committee and followed the European Communities Council Directive of 24 November 1986 (S6 609 EEC) and National Institutes of Health guidelines for care and use of animals for experimental procedures.

Behavioral paradigms

Two different arm movement tasks were used to probe the relationship of a cell to reach movements. The first of the two tasks in this study is identical to the delayed reach task used by Werner et al. (1997a) to identify reach-related neurons in the SC. Here we name it "saccade-reach" (SR) task in contrast to the second task, the "fixation-reach" (FR) task. The general outline of the two tasks is shown in Fig. 1. Both the SR and the FR task begin in the same way. The monkey has to touch a metal bar and to fixate a fixation light appearing on the screen. After a randomized interval (1–1.4 s), a target light was turned on. From here on the two tasks differed. In the SR task, the fixation LED was extinguished after a randomized delay (0.5–0.9 s). In response the monkey made a saccade to the illuminated target and fixated it (Fig. 1, *left*). After a second randomized delay (0.5–1.4 s), a tone came on that instructed the monkey to reach toward the fixated target. In the fixation reach task, the starting cue for the arm movement (the acoustic GO signal) was given after a randomized delay (1–1.4 s) while the fixation light on the screen remained on. The monkey had to maintain fixation while he reached to the peripheral target (Fig. 1, *right*). After touching the target for ~1 s, the monkey returned its arm to the initial starting position at hip level and received a liquid reward. The delayed saccade task and the two reach tasks were all performed in alternating blocks of at least five trials.

The targets for the arm movements were an array of eight metal knobs, each containing an LED. For the first monkey (*monkey C*), the eight targets were arranged on a circle with a radius of 15° centered on the fixation point at the monkey's eye level. For the second monkey (*monkey S*), the fixation light could appear at three sites, i.e., either centrally (F1 like in *monkey C*) or 19° lateral from the body midline (F2) or 19° below eye level (F3). Here the eight targets were arranged at a distance of 15° on the four corners of three squares around the fixation points. The knobs located between fixation points provided a reach target during fixation of either (see Figs. 4 and 6, scheme in the *bottom right corner*). Both arrays allowed to compare neuronal activity while the stimulus was at the preferred extrafoveal

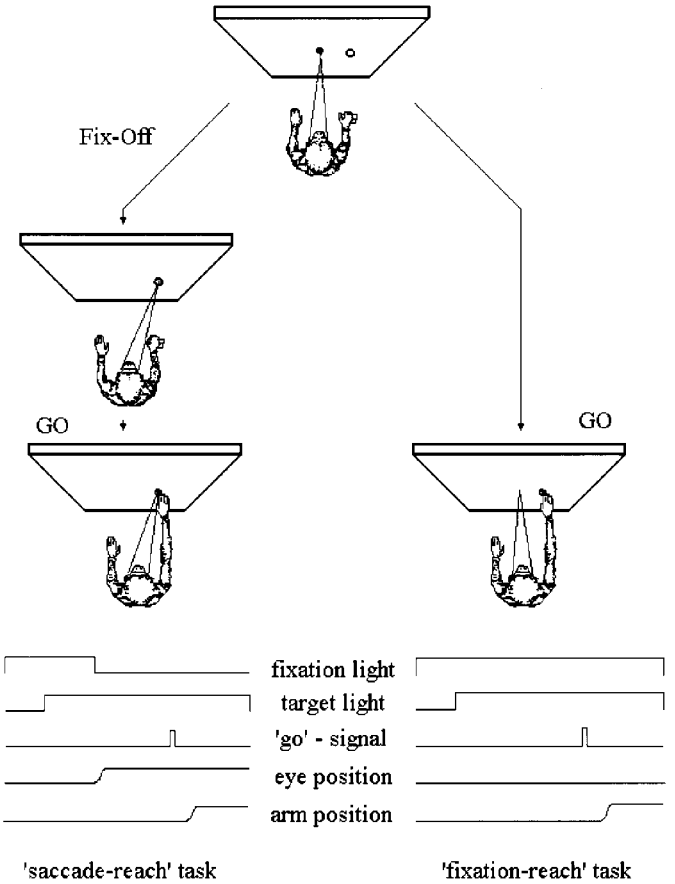

FIG. 1. Sequence of events in the reaching tasks. *Left*: saccade-reach task. *Right*: fixation-reach task. Temporal succession of the signals in both tasks is shown below. For details, see METHODS.

position with the activity while the target was at the fovea to calculate the gaze dependency index (see following text). In both tasks, the monkey received a liquid reward after correctly finishing the trial. The monkey's eye position was recorded and controlled throughout the task. During the fixation periods, the monkey had to maintain its gaze within a window of ±2.5° surrounding the light. If the monkey did not fulfill these criteria, the task was aborted and a new trial was started. The touch and release of the touchbar and reach targets caused a digital pulse that was used as a behavioral trigger event. These events were used for the on-line control of the animal's behavior as well as stored on computer disk.

In addition to these two reach tasks, we also used a simple delayed saccade task as an initial test of whether a newly isolated neuron had a relationship to eye movements.

During recording days, the monkeys only received liquid (water or apple juice) in the experiments and worked until satiated. After the experiments, the monkeys were returned to their home cage where they could socialize with other monkeys kept in the same group. The weight and overall health of the monkeys were monitored carefully, and on days without recording, free access to water was allowed.

Surgery

After training in the reaching task, the monkey was anesthetized with ketamine hydrochloride (10 mg/kg im) followed by pentobarbital sodium (25 mg/kg iv). Atropine (1 mg) and supplementary doses of pentobarbital sodium were administered intravenously. Under aseptic conditions, a stainless steel head holder was implanted on the animal's skull, and a recording cylinder was placed on the midline over the occipital pole, tilted backward 45° from the

vertical. Search coils were implanted under the conjunctiva around each eye (Fuchs and Robinson 1966; Judge et al. 1980). Electrocardiogram, body temperature, blood pressure, and SPO_2 were monitored during the surgery. Analgesics and antibiotics were delivered postoperatively for 1 wk.

Recording

Extracellular recordings of single neurons were made with glass-insulated tungsten electrodes (2–3 MΩ). The electrodes were lowered by a microdrive (Narishige) within a guide tube through the dura. The microdrive was mounted on the chamber whereby the electrodes penetrated the SC layers approximately perpendicular due to their 45° forward angle. Single-unit discharges were separated using a time-amplitude window discriminator and sampled with 1-ms time resolution. The collicular surface, which could be identified reliably by vigorous neuronal responses to visual stimuli presented at specific locations in the contralateral visual field, provided the reference point for the coordinates of the penetration. The depth of the hydraulic drive and the coordinates of the visual receptive field were noted. Then the electrode was advanced further through the midbrain while the monkey performed arm movements. We tested each well-isolated unit with the SR and FR task whether its discharge was related to arm movements.

Eye position was measured with a magnetic search coil system (Remmel). Separate horizontal and vertical eye position signals were sampled with a frequency of 500 Hz. These eye-position signals also were used to ensure a stable fixation during the tasks. Figure 2 indicates that this was indeed the case. It gives an example of the eye position recordings during both tasks from the second monkey. The data are not corrected for inhomogeneities in the magnetic field. Figure 2*A* shows the saccades in the SR task from a central point toward the eight targets, whereas in the FR task, the gaze clearly remains on the three fixation points (Fig. 2*B*).

Electromyographic (EMG) activity during the tasks was recorded differentially with intramuscular wire electrodes (0.05 mm diam, Teflon coated) that were inserted transcutaneously with hypodermic needles (27 gauge) under topical application of a local anesthetic (Xylocain). The EMGs were band-pass filtered and rectified before storage. The following muscles were recorded simultaneously with the neurons: M. biceps brachii (Bic), M. deltoideus anterior (ADl), M. deltoideus medialis (MDl), M. deltoideus posterior (PDl), M. infraspinatus (Inf), M. latissimus dorsi (Lat), M. pectoralis (Pec), M. rhomboideus (Rho), M. sternocleidomastoideus (Ster), M. supraspinatus, M. teres major (TMj), M. trapezius (Trap), M. triceps (Tri).

All the recorded data (behavioral events, eye position, neuronal discharge, EMG) were fed into an interface (CED 1401+, Cambridge Electronic Design), converted into digital data, and stored on a computer disc.

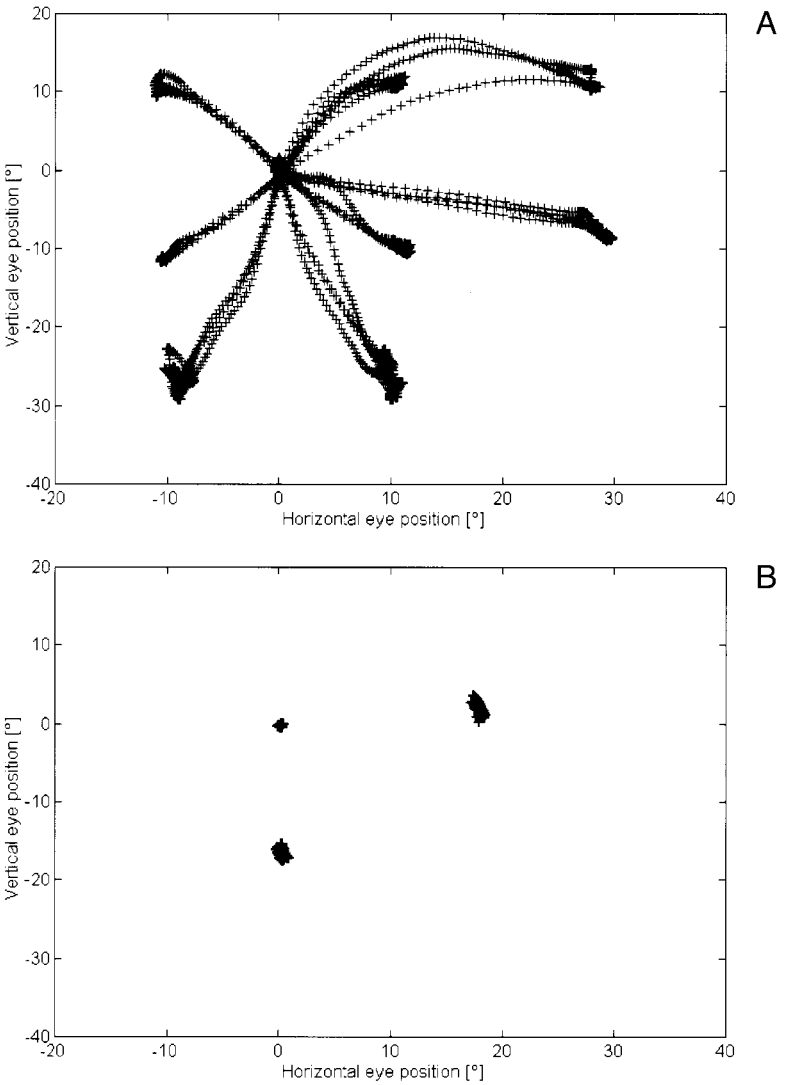

FIG. 2. Examples of eye positions in the 2 reaching tasks from the onset of the fixation light until contact with the arm movement target. *A*: eye positions in the saccade-reach task showing examples of saccades from the central fixation point toward the 8 different targets. *B*: eye positions in the fixation-reach task showing the fixation of the 3 fixation points while the monkey reaches to the targets around these fixation points.

Data analysis

Average time histograms of neuronal activity triggered on different behavioral events were accumulated routinely and visually inspected to classify cells as members of the following classes: visual (V), saccade-related (S), fixation (F), and reach-related (R) neurons. The discharge of reach-related cells was analyzed from the GO cue to target contact (over the combined reaction and movement time). All reach-related discharges in the SC occurred in this time window. To quantify the neuronal activity, we first counted the action potentials during this time period and then calculated the firing frequency by dividing the count by the appropriate time interval in each trial. We did the same trial-by-trial analysis for a time window of 500 ms preceding the GO signal. To qualify as a reach-related neuron, the mean firing frequency in the period after the GO cue until the end of the arm movement had to be significantly higher than the mean firing frequency in the preceding time period (Whitney-Mann, $P < 0.01$). We also determined the mean rectified EMG during this period as a measure of muscular activity.

We computed both a two-way ANOVA ($P < 0.01$) and a gaze-dependency index (GD) to quantify the extent to which a given cell operates in a gaze-centered or in a gaze-independent reference frame. The basic rationale of the comparison was the same for both measures. We compared two arm movements starting from and ending at identical positions in external space. What differed in the two cases was the direction of gaze with respect to the target. In one case (measured during the FR task), the gaze was directed away from the reach target, whereas in the other case (measured in the SR task), the gaze was aligned on the target. Because the two compared arm movements were identical, any systematic change in reach-related cell activity should be a result of the difference between target and gaze axis in the two cases. As mentioned before *monkeys C* and *S* were tested with slightly different target displays. The display for *monkey C* used only one fixation point and thus did not provide us with comparable mappings from different fixation positions as in *monkey S*. Nevertheless for both displays, we had data recorded during identical reach movements while the monkey's gaze axis was aligned with the reach target (SR task) as well as while it was directed away from the reach target (FR task).

The ANOVA was computed to test if there was a systematic influence of gaze across the different arm movements. The data for the ANOVA were the average neuronal firing frequency from the GO cue to the end of the arm movement in the individual trials. The factors for the ANOVA were the craniocentric target position (which is related to the arm reaching movement toward a certain position in the workspace) and gaze direction (either pointing to the target or to the central fixation light).

The GD was computed to quantify the amount of modulation of the neuronal discharge during the reach caused by the gaze shift. GD was calculated in the following way. First, we determined the target with the maximal reach activity (the mean of the firing frequency from the GO cue to the end of the arm movement over the individual trials) of the neuron in the FR task condition. We took this target location to be the preferred gaze-target vector (GTV_p). Second, we determined the neuron's discharge while the monkey reached to the identical target on the screen, but this time in the SR task, in which the monkey fixated the target before and during the reach. This gaze orientation resulted in a gaze-target vector that was zero (GTV_0). We compared the two situations by calculating the GD index

$$GD = \frac{GTV_p - GTV_0}{GTV_p + GTV_0} \quad (1)$$

The same analyses also were performed with the muscle activity.

To reconstruct the spatial relationship of the reach neurons among each other, we used the visual receptive field, measured in the same penetration during the passage of the superficial layers, to estimate the position of the neurons on a reduced SC map. We used the equations of Ottes et al. (1986) to relate collicular and retinotopic coordinates.

To compare the average discharge modulation in the two reach cell populations (gaze-dependent and -independent), we computed histograms of their population activity during the FR task. To eliminate the trial-by-trial variation in the duration of different behavioral elements in the FR task, we divided these elements into a fixed number of bins that remained the same in each trial. The FR task was divided into five successive behavioral elements. First, the "waiting phase" (50 bins) lasted from fixation onset until target onset. Second, the "delay phase" (60 bins) lasted from target onset until the acoustic GO signal was given. Third, the "reaction time" (20 bins) lasted from the GO signal to onset of the arm movement. Fourth, the "movement phase" (10 bins) lasted from onset of the movement until the hand made contact with the target. Fifth, the "target hold phase" (35 bins) finally lasted from contact with the target until its release at the beginning of the return movement. The number of bins for each phase was chosen in such a way that one bin accounted on average for ~20 ms. The actual time represented by such a bin could vary with the duration of the respective phase in the trials. Therefore the activity in a certain bin does not represent the mean activity in real time relative to a trigger point but rather the mean activity at a certain fraction of the respective behavioral element. For example the first bin of the MP shows the average discharge during the first 10% of the arm movement. Therefore we called the resulting histograms "relative time histogram" (RTH).

RESULTS

Classification of neurons

In two monkeys, we recorded 331 neurons in the SC and the underlying mesencephalic reticular formation (MRF) over a depth from 1 to 6.5 mm below the SC surface. These neurons were classified with respect to the relationship of their discharge to the visual cues and the eye and arm movements as visual (V), saccade-related (S), fixation (F) and reach-related (R) neuron (see Table 1).

Sixty-five neurons with reach-related activity provided sufficient data for quantitative analysis. Four examples of them are shown in Figs. 3 and 4. All of them showed a burst of activity at the time of the arm movement. However, the start and end of this burst varied in individual cells. It began at some point in the interval between the GO cue (Fig. 3*A*) and the onset of the reaching movement (e.g., Fig. 4*A*). The burst ended

TABLE 1. *Number and proportion of recorded neuron types in two monkeys*

	Monkey C	*Monkey S*	Total
Recorded cells	232	99	331
Visual cells (V)	18 (7.76)	6 (6.06)	24 (7.25)
Saccade-related cells (S)	48 (20.69)	7 (7.07)	55 (16.62)
Fixation cells (F)	6 (2.59)		6 (1.8)
Reach-related cells (R cells)	95 (40.95)	52 (52.53)	147 (44.41)
R cells tested in FR + SR task	32	33	65
Gaze-related R cells	20	5	25
Gaze-independent R cells	12	28	40
Others	65 (28.02)	34 (34.34)	99 (29.91)

The number and proportion (expressed as percentages) in parentheses is given for all identifiable neurons that were recorded in *monkeys C* and *S*. FR and SR, fixation and saccade reach, respectively.

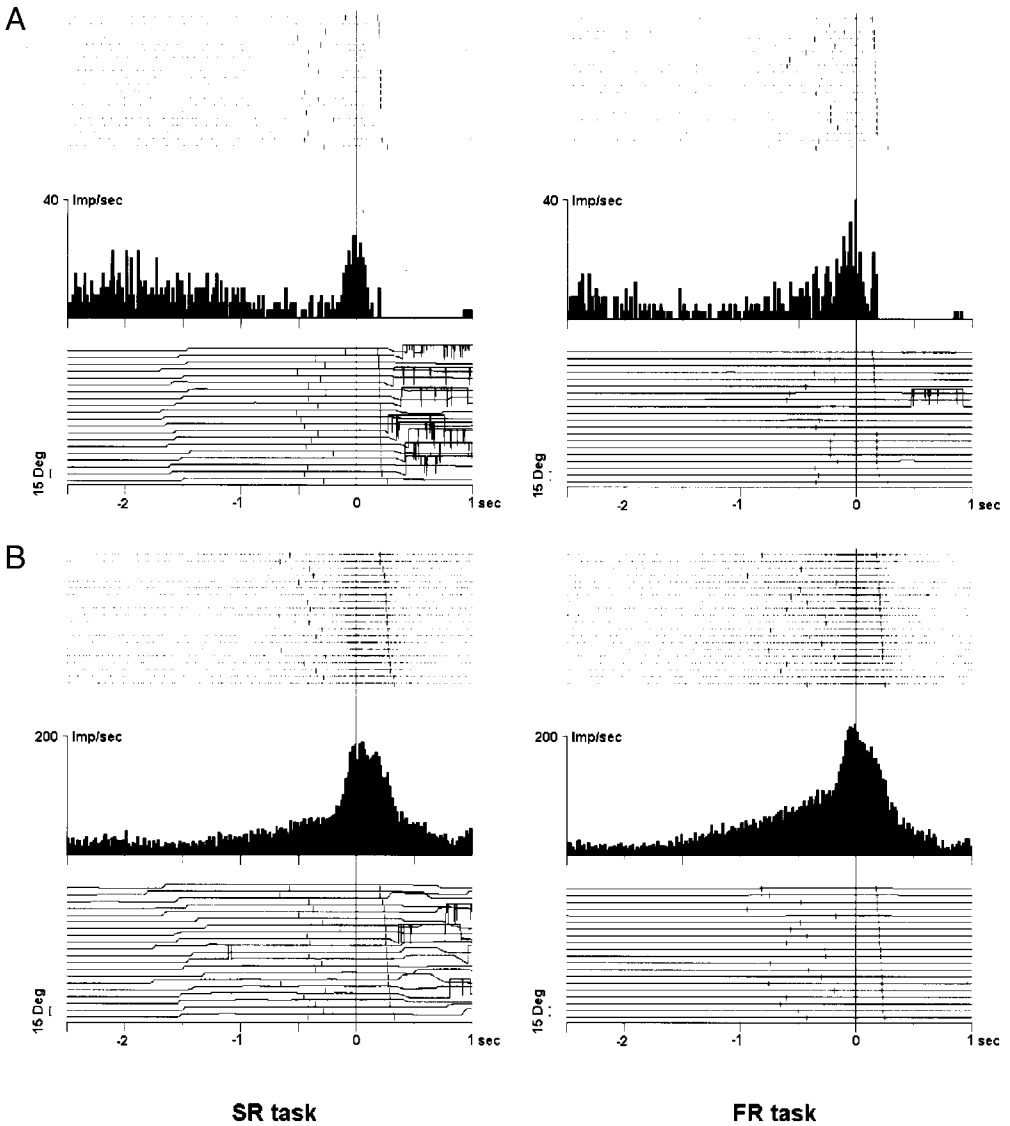

FIG. 3. Neuronal activity and eye position recording of 2 gaze-independent reach neurons in the saccade reach (SR) and the fixation reach (FR) task. For each of the cells, the data on the *left side* represent trials in which the monkey reached to a target during the SR task. Data on the *right side* represent trials in which the monkey reached to the same target during the FR task. For all cases, the discharge of the neuron in each trial is given in a raster plot; each dot is the occurrence of an action potential. Averaged activity is presented in the histograms (20-ms bins). Horizontal eye position traces in each trial are shown *below* the neuronal activity. Data are aligned on the onset of the arm movement (vertical line at $t = 0$). Short vertical lines to the *left* in the raster and the eye position show the times of the appearance of the GO signal for the arm movement and to the *right* of first target contact. Trials are ordered according to increasing movement duration. Neurons display no saccade-related activity and both show the same reach-related activity during both tasks.

either while the movement was still ongoing (Fig. 3*A*) or, more often, when the monkey had grasped the target handle (Fig. 4*B*). Some neurons displayed also an additional modulation in the delay interval preceding the arm movement. This delay modulation was often more pronounced in the FR task and could be either an inhibition (Figs. 3*A* and 4*A*) or a ramp-like increase (Fig. 3*B*) of the discharge.

The great majority of the reach-related cells (86.1%) showed no modulation related to saccades. This is in accordance with earlier findings by Werner et al. (1997b).

Besides many similarities, a comparison of the discharge modulation in the SR and the FR tasks also revealed a clear difference between two different types of reach-related cells. On the one hand, there were cells like the ones shown in Fig. 3 that show no or only slight differences in their discharge during the actual arm movement in the two tasks. Because the arm movement was the same in the two cases, this finding was not unexpected. On the other hand, we found also cells like the ones shown in Fig. 4 the discharge of which was dramatically different depending on which task the monkey performed. Because the arm movements were identical, this difference had to be related to the difference in gaze angle.

To determine quantitatively this effect of the gaze-related target coordinates on the reach activity, we computed a GD index. This index equals ± 1 if the activity occurred only during one of the two compared arm movements and therefore depended maximally on the direction of gaze. If, on the other

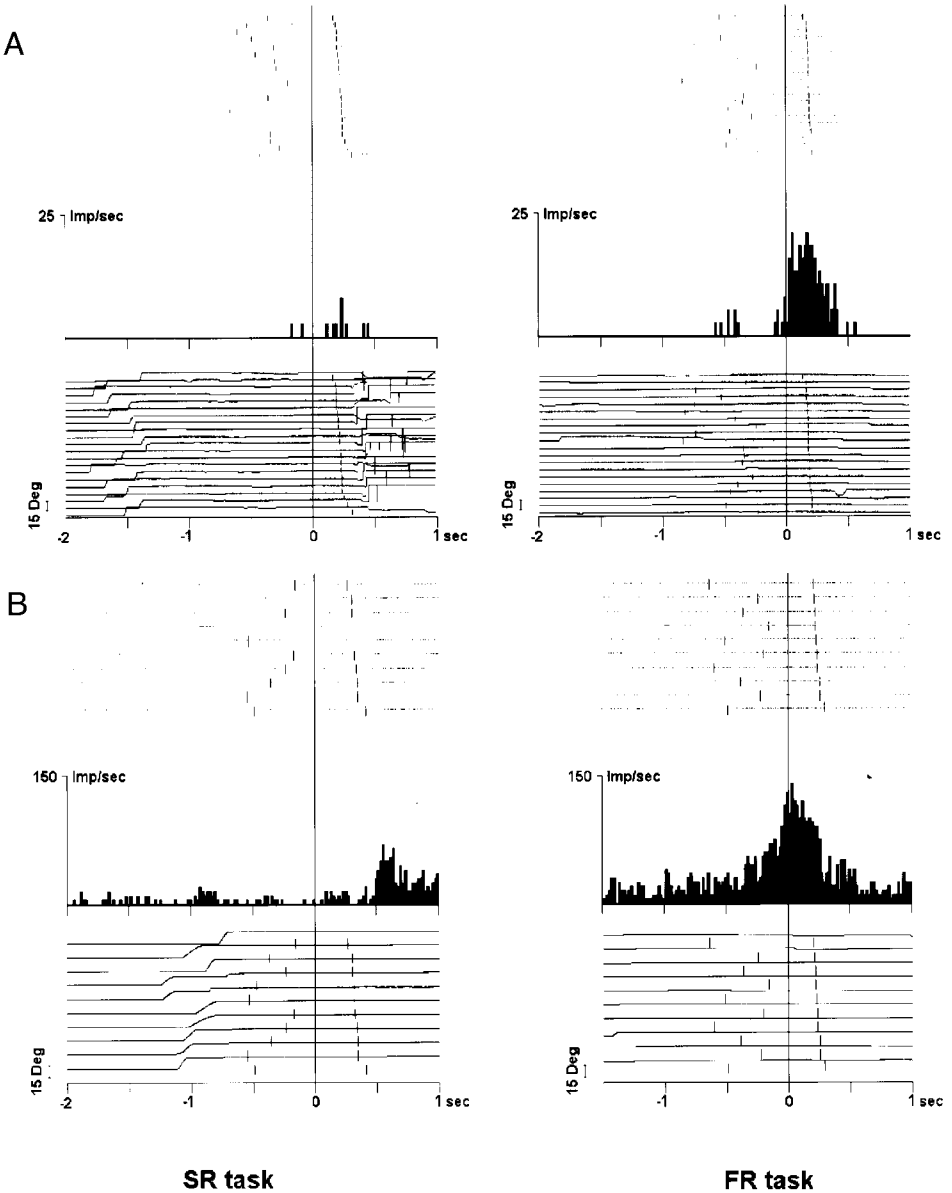

FIG. 4. Neuronal activity of 2 gaze-related reach neurons and eye position recording during the SR and FR tasks. Figure is arranged in the same way as Fig. 3. Neurons display no saccade-related activity just as the cells shown in Fig. 3, *A* and *B*. Note, however, that the neurons displayed here are only active during the FR task in contrast to those in Fig. 3.

hand, the index equals 0, the activity is not modulated by gaze angle and therefore seems independent of it. In addition to this index we computed also a two-factor ANOVA (craniocentric target position, gaze direction, $P < 0.01$).

The monkeys might perform the arm movements in a slightly different manner in the SR and the FR task. This could result in different activity patterns of the musculature in the two movements compared. To estimate the amount of difference, we also computed the GD values of the rectified and averaged EMGs from representative shoulder and arm muscles made simultaneously with the neuron recordings. The GD distribution of these muscles gives an estimate of the amount of change that the gaze shift produced in the skeletomotor system. A comparison of muscle activity from the deltoideus anterior (Adl) during arm movements toward targets at identical locations with respect to the body but with different coordinates with respect to gaze direction (e.g., toward target 5 while looking at fixation point F1, F2, and F3, respectively) is shown in Fig. 5. Clearly, the EMG patterns display almost the same amplitude and shape during identical reach movements with different gaze angles.

In Fig. 6 the GD distributions of the muscles and the neurons are shown for comparison. Figure 6*A* gives the mean GD values of the 13 muscles. The unimodal distribution clearly is centered on zero, and values do not exceed ± 0.3. In the ANOVA none of the muscles showed an effect of the gaze angle during reaching. Figure 6*B* shows the GD values of the 65 reach neurons. The units for which the ANOVA ($P < 0.01$) showed a significant influence of gaze angle are shown in black. In 27 cells the GD falls outside the range of the muscle modulation and exceeds ± 0.3, corresponding to twice the activity in case of preferred as compared with nonpreferred gaze-related target coordinates. All of these cells with the exception of two near to the 0.3 level are influenced significantly by gaze angle. We called the 25 (38.5%) cells that fulfill both criteria (ANOVA $P < 0.01$; GD $> \pm 0.3$) "gaze-related reach neurons." The GD values of the rest of the reach-related neurons ($n = 40$, 62.5%) fall into the same range as the GD of

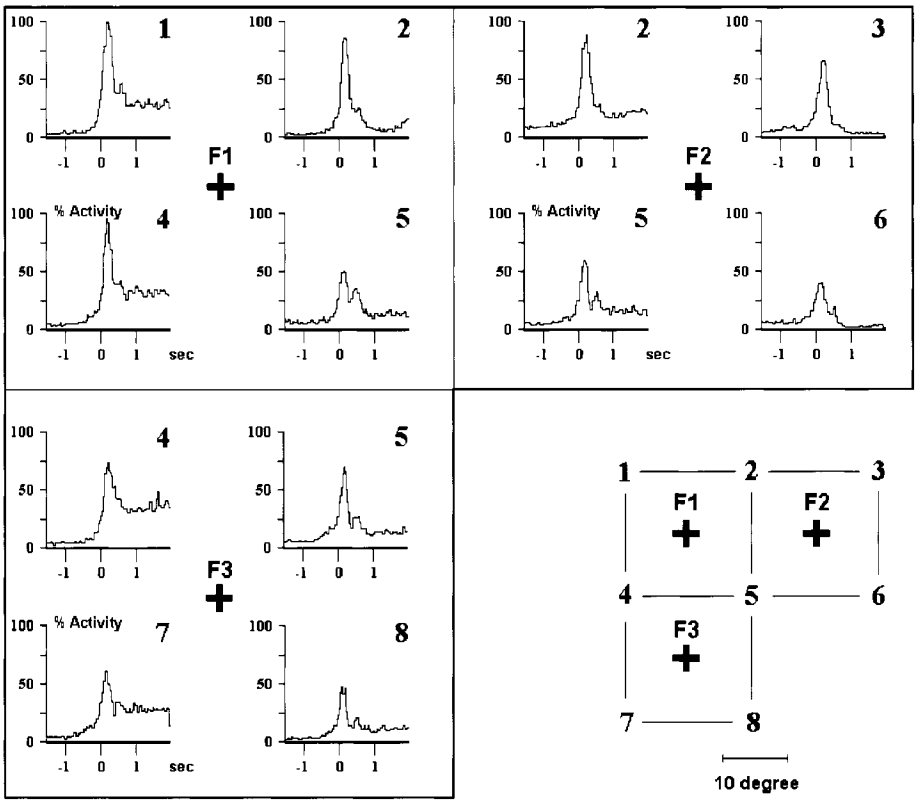

FIG. 5. Activity of a shoulder muscle, the M. deltoideus anterior in the fixation reach task. Monkey reached from 1 starting position to 8 targets (see scheme in the *bottom right corner*) during 3 different gaze directions. Monkey fixated a light spot (+) straight ahead (F1), at 19° to the right (F2), or 19° down (F3) from straight ahead and reached to the 4 targets surrounding each fixation point. Eight reach targets are arranged on a frontal screen in 3 squares, each with a fixation point in its center. The targets 2, 4, and 5 were in identical spatial locations but had different positions relative to the fixation points. Electromyographs (EMGs) during the resulting 12 combinations of gaze direction and reach target location are presented in 12 histograms compiled in sets of 4 around the 3 fixation points. Each histogram is constructed on the basis of 10 trials temporally aligned to arm movement onset.

the muscles, indicating that their reach activity is independent of retinocentric or eye-position variables. Although some of them showed a significant gaze influence in the ANOVA, we excluded them from the group of the gaze-related reach neurons because they did not fulfill the second criteria (GD $> \pm 0.3$). We called this second type of cells "gaze-independent reach neurons."

Characteristics of the gaze-related reach neurons

The typical activity pattern of a gaze-related reach neuron both in the SR and FR task is shown in Figs. 7 and 8. In Fig. 7 the discharge of this sample neuron is presented in relation to onset of arm movements in the FR task while the monkey uses either the ipsilateral or the contralateral arm. The 12 histograms on the *right* were compiled in sets of four according to the arrangement of four reach targets around each of the three fixation points (+). All movements were made with the contralateral (here the right) arm. They started with the hand approximately at waist level and were directed to one of the eight targets (1–8), positioned on a frontal screen as outlined in the sketch in the lower right corner of Fig. 7. Activation was observed only when the arm was directed to a target at the lower right with respect to the fixation point. This occurred with targets 5, 6 and 8. However, if the same arm movement (e.g., to target 5) was performed with eye positions that shift the target location with respect to the gaze axis, i.e., to the upper right or lower left the neuron displayed no reach-related activity. The neuron was also not active during reaching when the same eight targets were fixated in the SR task, as illustrated in Fig. 8.

Even for the same target location with respect to the gaze direction (see Fig. 7, targets 5 (F1), 6 (F2), and 8 (F3)) the cell discharge is different for the three different orbital positions of the eyes during the reach. This eye-position effect occurred across the tested oculomotor range for all gaze-related reach cells. We did not perform a quantitative description of these gain fields because we felt that three different gaze positions did not allow such a treatment of the data.

All these experiments demonstrate that the reach-related activity of this neuron is locked to a gaze-related coordinate system and cannot be described in an allocentric or body-centered reference frame. Nevertheless, its activity is in close temporal relationship to the arm movement, preceding the onset of movement by ~200 ms. We called the area of target coordinates in a gaze-related frame of reference that is accompanied by neuronal activity the "reach movement field" (RMF). It is important to note that both the specific path of the arm movement and the muscle pattern that is necessary for its realization are of no consequence for the neuron's discharge. Two neurons of the 25 gaze-related neurons also produced saccade-related bursts, but we found no relationship between these components and particular characteristics of the reach-related activity.

Activity of the gaze-related reach neurons during reaching with the contra- or ipsilateral arm

To see whether the reach neurons show a preference for the use of the arm contra- or ipsilateral to the recorded SC neuron, we let the monkey perform the FR task with either arm. Because of workspace constraints, we could compare only the movements that were in a medial position with respect to the body axis while the monkey fixated the fixation points F1 and F3. The fixation point F2 was on a more lateral position and included movement targets that could not be reached with the

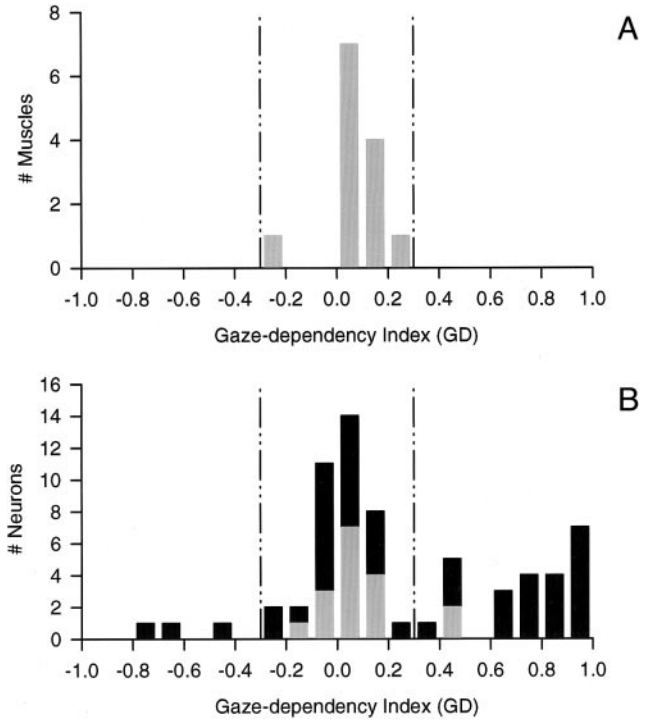

FIG. 6. Gaze-dependency (GD) index and significance of gaze influence (ANOVA) of neurons in the superior colliculus as well as of arm and shoulder muscles. For computation of the GD index, see METHODS. In short, activity amplitudes were compared between arm movements aimed at identical targets located either at a preferred or a nonpreferred position with respect to the gaze axis. *A*: GD distribution of the electromyograms from 13 representative muscles recorded simultaneously with the neurons is shown as a reference for the GD values of the neurons. GD values of the muscles are centered around 0 and did not exceed ±0.3. *B*: GD distribution of 65 reach-related cells. One group of cells ($n = 40$) had GD values in the same range as the EMGs of the muscles; this indicates reach-related activity at least as independent of gaze direction as the muscles or showed no significant gaze influence by the ANOVA (▤). Another group of neurons ($n = 25$) with GD values >±0.3 and a significant gaze influence (■) were tuned for reaches to targets with a certain location in relation to the gaze axis. Three neurons of this group showed activation predominantly during arm reaching to targets located on the gaze axis (GD > −0.3).

left arm. In Fig. 7*A*, the activity of the same cell that was discussed in the preceding text in the case of reaching with the contralateral (right) arm is shown also during use of the ipsilateral (left) arm. A comparison of the neuronal discharge histograms reveals that the neuron displays the same pattern of activity with an identical spatial tuning and almost the same amount of spikes irrespective of which arm is used although anatomically different muscles execute the reach movements. A further demonstration of the similarity of the activity level during reaches into the RMFs with the ipsilateral or contralateral arm is shown for eight neurons in Fig. 9. Each dot shows the mean neuronal activity for one of the eight neurons while the monkey reached to the "preferred" targets surrounding the fixation points F1 and F3 (see Fig. 7). The plot basically confirms the points taken from the example shown in Fig. 7. Only in one of the eight neurons was the difference between the activity during the reach with the contra- or ipsilateral arm significant (triangle pointing down; *t*-test Bonferroni corrected: $P < 0.05$). Otherwise there are just as many values on either side of the unity slope line. All in all, a population of gaze-related reach neurons in the colliculus becomes activated during a goal-directed reach largely independent of the muscles or arm involved in the reach.

RMFs

We found that the RMFs of gaze-related reach neurons differed with respect to their peripheral borders. In six neurons, the RMFs were mapped partially by presenting reach targets further and further away from the preferred retinal target position. Figure 10 shows two examples of these cells. Neuronal discharge of the cells is shown while the monkey fixated a certain position on the screen (the cross) and reached to a number of targets (indicated by position of the histograms). The amplitude of reach activity increased when the monkey was reaching to more peripheral targets in the cell presented in Fig. 10. This suggests that its RMF occupies a large area of the visual field and may possibly have no clear peripheral border at all. Such patterns of neuronal activation were seen in four of the six neurons tested. The other two cells allowed no clear conclusion due to the limited number of tested locations. In addition to these cells, we also recorded three neurons with a GD value more than −0.3 (Fig. 6*B*). This GD index resulted from a strong activation of the neurons in the SR task coupled with a weak discharge during reaching to targets falling outside the fovea. An example of these cells is shown in Fig. 11. In Fig. 11*A*, the neuronal activity during reaching to the four targets surrounding the F1 fixation point in the FR task is displayed. In Fig. 11*B*, we see the neuronal discharge while the monkey reached to the same targets during the SR task. Obviously, the cell is much more and always activated when the target falls on the gaze axis. Another observation is the identical amplitude of the discharge for all spatial positions in the SR task. Because the arm movements are the same in the two tasks, once again the difference in response must be due to the gaze-related target position. These neurons seem to have RMFs that are positioned on the fovea and peripheral borders of which lie somewhere between the fovea and the targets with an eccentricity of 15°.

Distribution of RMF orientation on the SC

For the 25 gaze-related neurons (ANOVA $P < 0.01$; GD > ±0.3), the direction and spatial selectivity of the RMFs was assessed quantitatively by constructing the vector sum of the normalized neuronal activity during reaching to each of the four targets. The orientation of the resulting vector pointed toward the RMF of the cell. Vectors pointing into the contralateral hemisphere were indicated by a rightward orientation. The length of the vector increases with a sharper spatial selectivity of the cell.

To test whether there is a map-like arrangement of the RMFs of gaze-related neurons parallel to the collicular surface, we plotted these vectors on the simplified visual map of the SC (see Fig. 12). To construct this map, we used the equations of Ottes et al. (1986) to plot the anterior-posterior and mediolateral position of a reach neuron in the SC according to the coordinates of the visual receptive field measured in the same penetration during the passage of the superficial layers. The reach cell's location according to this visual map serves as the origin of the respective RMF vector. The RMFs of the gaze-related reach neurons could be directed either into the ipsi- or

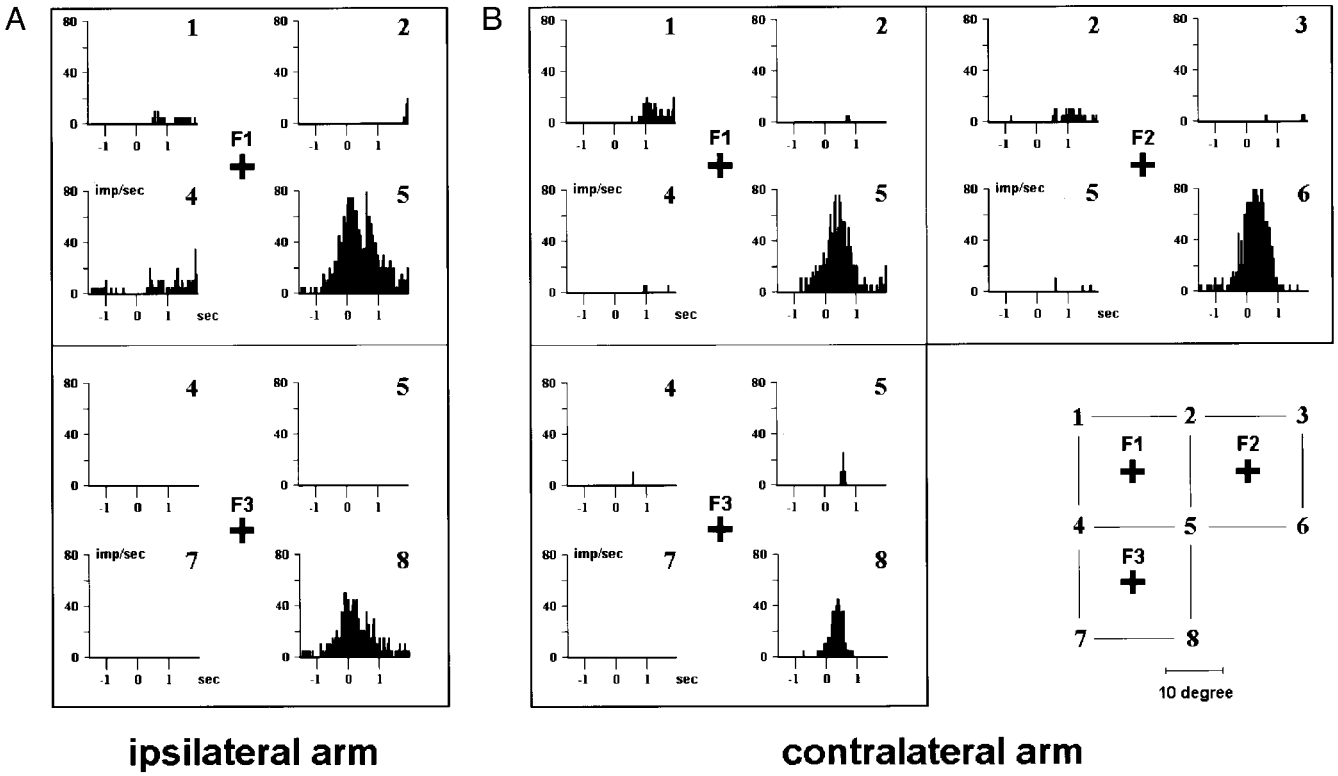

FIG. 7. Activity of a gaze-related reach neuron in the fixation reach task. Cell was recorded 1.96 mm below the surface of the left colliculus. Histograms to the *left* (*A*) show the neuronal activity while the monkey used his arm ipsilateral to the recorded colliculus, whereas the ones on the *right* (*B*) show the neuronal activity while the monkey used his contralateral arm. Activity pattern was the same irrespective of which arm was being used. Figure has exactly the same arrangement as Fig. 5, showing the activity of a shoulder muscle. Histograms are aligned on arm movement onset ($t = 0$). Neuron was always active if the reach aimed toward a target down and to the right from the direction of gaze (target 5 with F1, target 6 with F2, and target 8 with F3); however, the cell was completely inactive during arm movements toward the identical targets in space when gaze shifts produced an altered relation between reach target and gaze axis (e.g., target 5 with F2 and F3). Therefore the cell operates in a coordinate system centered on the gaze axis.

the contralateral hemifield, i.e., the preferred reach target location could be in the entire visual field and was not restricted to the contralateral hemifield; this is in sharp contrast to the organization of the visual map and saccadic movement fields. In addition, gaze-related reach cells recorded in a single penetration next to each other repeatedly showed clearly different RMF positions. But a closer inspection of Fig. 12 might reveal a weak organizing principle. The subpopulation that was recorded in the medial part of the colliculus corresponding to the upper visual field consisted mostly (8/13) of cells with RMFs also oriented upward. Correspondingly, the lateral part of the SC was dominated by gaze-related reach neurons with downward oriented RMFs (8/12). All seven reach cells recorded within 5° eccentricity to the foveal representation had RMFs directed into the ipsilateral hemifield, whereas 13 of the 18 reach cells recorded in penetrations with visual fields with >5° eccentricities had RMFs directed into the contralateral hemifield.

Gaze-independent neurons

The other group of units analyzed in detail consisted of 40 neurons that showed no or only a weak dependence of their discharge on the orientation of the gaze axis (ANOVA $P > 0.01$ or GD $< \pm 0.3$). An example of such a gaze-independent neuron is given in Fig. 13. The pattern of discharge is the same

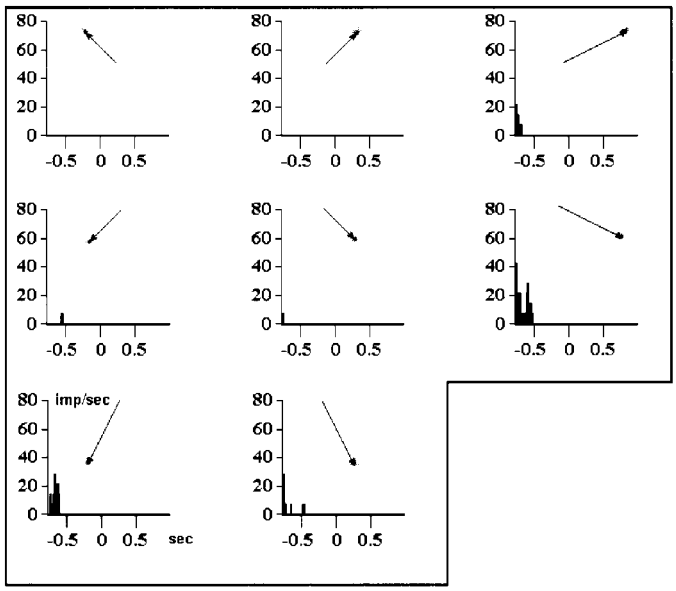

FIG. 8. Activity of a gaze-related reach neuron in the saccade reach task. Cell is the same as the one shown in Fig. 7. As in the previous figure, the histograms are aligned on arm movement onset ($t = 0$). Vectors pointing to the crosses indicate the direction and amplitude of the saccade with which the monkey shifted his gaze to the reach target (cross). Cell was never activated if the 8 reach targets were fixated during the arm movements.

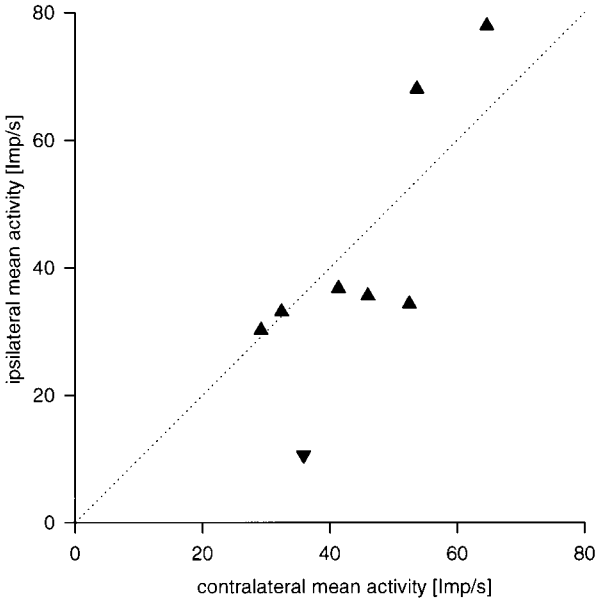

FIG. 9. Mean activity of gaze-related cells during use of the ipsi- and the contralateral arm to reach to the same target in space in the FR task. In the plot, data from 8 neurons are displayed. Each data point represents the mean neuronal activity of 1 neuron while the monkey reached into the reach movement field of that neuron. ▲, neurons with similar activity irrespective of the arm being used; ▼, neuron with a significant ($P < 0.05$) difference. Activity during the reach with the contralateral arm is presented on the *x* axis and during the reach with the ipsilateral arm on the *y* axis. Note that the neuronal activity of the gaze-related neurons is largely independent of the arm used to perform the movement.

in the fixation and saccade-reach task, although the neuron shows a modulation of its activity in relation to the four target positions.

We computed the orientation of the RMF vectors in the same way as for the gaze-related neurons and plotted them on the oculomotor map of the SC (Fig. 14). This reveals two points. First, the gaze-independent cells show an even less ordered distribution across the SC compared with the other group of reach cells. Second, the tuning sharpness as visualized by the vector length is much weaker than the corresponding values of the gaze-related neurons.

Discharge dynamics of gaze-related and -independent reach neurons

To compare the discharge dynamics and directional modulation depth of the two reach-related populations, we compiled RTHs of the activity of the reach neurons during the FR task for the gaze-dependent and the -independent populations separately. First we computed for each neuron a relative time histogram of the averaged activity for all recorded arm movements toward a certain target in the FR task. Then for each neuron from its pool of histograms we chose the two associated with the maximal and minimal response. Next we calculated separate population histograms for the maximal and minimal activities.

The gaze-independent neurons (Fig. 15*A*) show on average a smooth increase of their discharge, starting in the delay period (after target on) before the GO cue is given. At this moment the monkey has all the information that is needed to perform the arm movement and is merely waiting for the start signal. Thus the activity during this time probably reflects the expectation and preparation to execute the planned movement in the near future. Examples of gaze-independent neurons with anticipatory activity components can be seen in Figs. 3*B* and 13. The discharge dynamics in the case of maximal and minimal activity are the same. The peak in the maximal activity gets about twice as high as the peak in the minimal activity.

The picture is very different for the gaze-related neurons (Fig. 15*B*). First, the maximal discharge amplitude of the gaze-related cells is nearly twice as high as the one of the gaze-independent cells (153.5 vs. 81.9 imp/s). We found no gaze-related neurons with delay activity preceding the command to reach to the target. The rise of the discharge begins only after the GO cue is given. At this point, the slope of the rise is comparable with that in the gaze-independent neurons. With movement onset, the slope dramatically increases, which leads to a brisk burst of discharge, lasting until the arm makes contact with the target. In contrast to the course of the maximal discharge, the minimal activity is nearly negligible over the equivalent time span.

Depth of gaze-related and -independent reach neurons below the surface of the colliculus

The depth distribution of the two types of reach-related neurons is shown in Fig. 16. For comparison, the depth distribution of the saccade-related neurons as recorded in our experiments also is shown. We could not reconstruct the position of single neurons in the histological sections of the SC, because after 1.5 (*monkey C*) and 1 yr (*monkey S*) of recording it was not possible anymore to identify single penetration tracks. However, in *monkey C* we made lesions at the position of two gaze-independent reach neurons during the last week of recording. The depth below the surface of the SC of both lesions matched very well with the depth recorded by our microdrive. Further histological verifications of reach cells in the SC are given in a previous publication (Werner et al. 1997b). We recorded the gaze-related reach neurons in the SC at depths of 0.9–3.6 mm with a median of 2.02 mm (Fig. 16*B*). They mostly overlap with saccade-related burst neurons recorded in the same penetrations over a range of 0.8–3.0 mm (plus 2 units at 5 mm) with a median depth of 1.55 mm (Fig. 16*A*). Thus the gaze-related reach neurons seem to lie also in the intermediate layers interspersed with saccade-related neurons. By contrast, most of the gaze-independent reach neurons were found in a range of 1.3–6.5 mm below the SC surface with a median depth of 4.01 mm (Fig. 16*C*). If both cell types were found in individual penetrations, gaze-independent cells were mostly found below gaze-dependent cells.

DISCUSSION

This study demonstrates that the reach-related neurons in the SC and underlying MRF are composed of at least two functionally separable populations. Gaze-related reach neurons are located in the SC and overlap mainly with the depth distribution of the saccade-related neurons recorded in the same study. Gaze-independent reach neurons could be found in the SC, but a great number of them were located in the underlying MRF. The median depth of this population (4.01 mm) is 2 mm deeper than the median depth of gaze-related reach cells (2.02 mm).

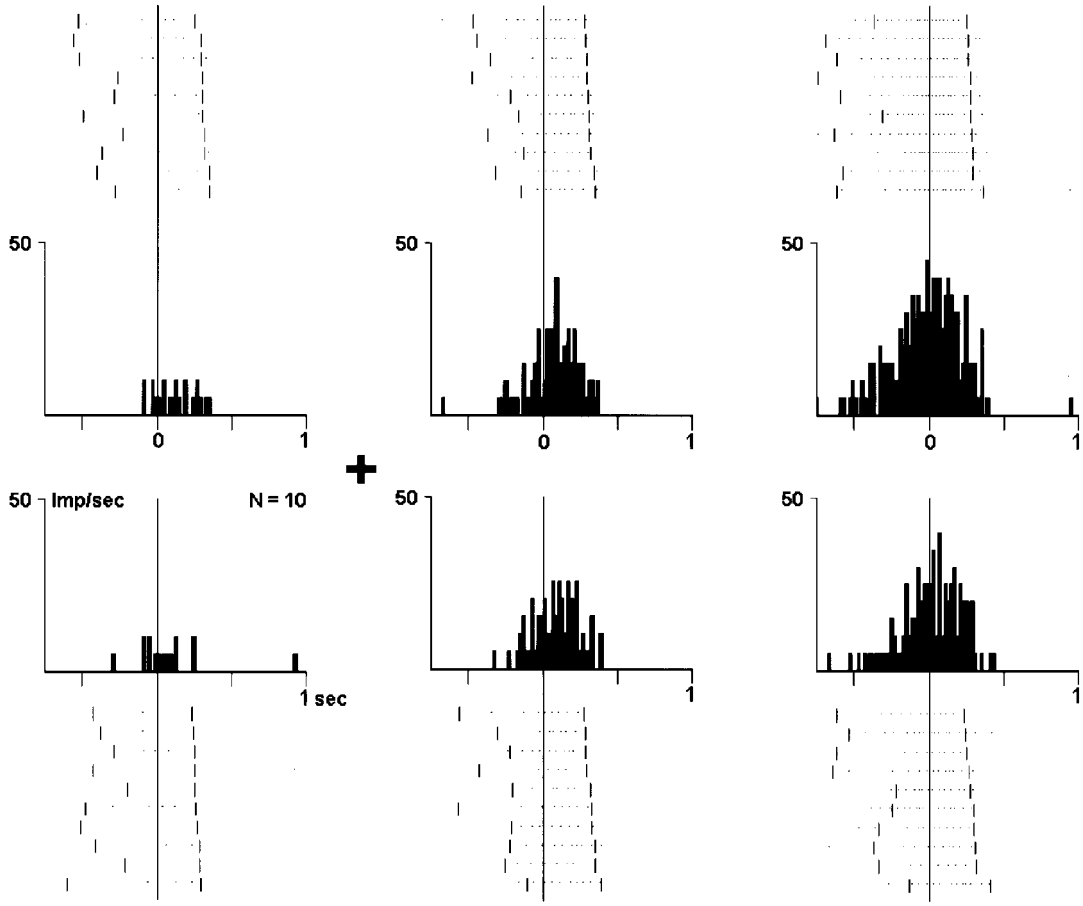

FIG. 10. Activity of a gaze-related reach neuron with a reach movement field without clear peripheral borders. Neuronal activity while the monkey reaches toward the targets surrounding the fixation point indicated by the cross is shown by raster displays and histograms. Discharge of the neuron in each trial is given by the raster where each dot represents the occurrence of an action potential. Averaged activity is presented in the histograms (20 ms bins) arranged around the cross like the targets around the fixation point. Data are aligned on the onset of the arm movement (vertical line at $t = 0$). Short vertical lines to the left in the raster show the times of the appearance of the GO signal for the arm movement and to the right of first target contact. Trials are ordered according to increasing movement duration. Note that the cell's discharge increased with targets lying to the right of the fixation point at more peripheral positions. There seems to be no border of the reach movement field (RMF) toward higher eccentricities.

These anatomically differently located two populations differ also in their frame of reference, their tuning strength, and the dynamic of their discharge modulation during the task. In another study, using only the SR task, arm-movement-related neurons were reported to be distributed between 0.7 and 6 mm below the SC surface with a median of 3.9 mm (Werner et al. 1997b), which is indistinguishable from our present result for the gaze-independent reach cells. In Werner et al.'s studies gaze-related neurons could not be identified because the animals were not trained to perform the FR task. Neither group of neurons shows a topographically ordered anatomic distribution matching the well-known visual or oculomotor maps in the SC (see Figs. 12 and 14).

The gaze-related reach neurons seem to be organized in a reference frame centered on the gaze axis. The discharge of the gaze-independent neurons might conform to a shoulder and arm-centered frame of reference. In this case, the strength of neuronal discharge would depend on the arm used to reach to the target. In this study, we did not test the activity of the gaze-independent neurons while the monkey was using his ipsilateral arm. However, Werner et al. (1997a) present such data in their Fig. 8 in support of a shoulder- or arm-centered reference frame. All of the 26 reach neurons they analyzed in their study showed a weaker activity (sometimes a decrease by 80%) when the monkey used its ipsilateral arm.

Function of the gaze-related reach neurons

The experimental setup we used in this study allowed us only a very broad mapping of the RMF structure of the gaze-related reach neurons. The distinction between neurons with closed or open RMFs therefore remains of a tentative nature. Nevertheless the gaze-related SC cells have spatially selective RMFs. For a given gaze position, this population of neurons would reliably signal reach target positions relative to the fovea. The motor system of primates could use this information under certain behavioral constraints, e.g., when a monkey, looking at a distant piece of food, at the same time is reaching out to climb up nearby branches or when one reaches for a pencil while reading a text. The main arguments against this interpretation result from the temporal pattern of activity of the gaze-related reach neurons. First, the activity of all these neurons begins to rise only with the GO cue and shows another sharp burst-like rise shortly before the arm movement onset

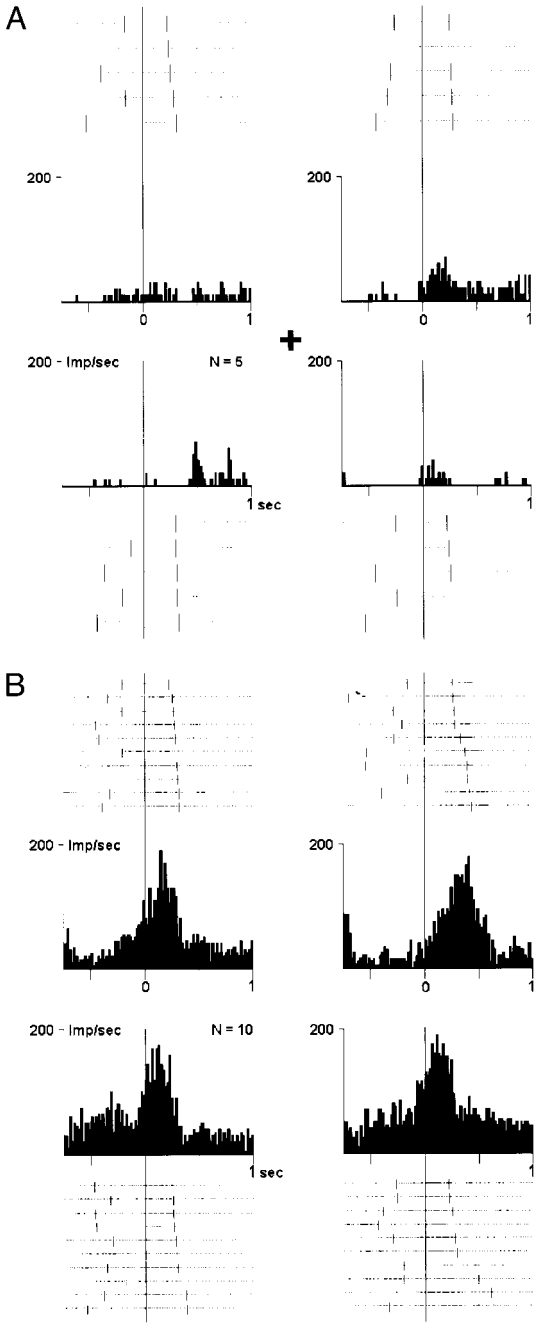

FIG. 11. Activity of a gaze-related reach neuron with a reach movement field located near to the fovea. As in Fig. 10, the activity of the neuron is displayed as raster plots and histograms (bin size, 20 ms). *A*: neuronal activity while the monkey reaches toward the targets with eccentricities of 15° surrounding the fixation point in the fixation reach task. *B*: neuronal activity while the monkey reaches toward the same targets in the saccade reach task. This time the monkey always fixates the targets while he reaches toward them. Note the great burst of discharge that has the same amplitude for all the arm movements to fixated targets.

that lasts over the movement time. This is not in agreement with the hypothesis that these neurons code the target location or the intention to move to the target because in that case these signals should be generated from shortly after the target onset until the execution of the movement. Neuronal activity in the parietal cortex indeed shows a continuous discharge starting with target onset in an instructed delay phase preceding a movement (Batista et al. 1999; Bushnell et al. 1981; Paré and Wurtz 1997; Snyder et al. 1998). Second, the population activity of the gaze-independent reach neurons begins to rise before that of the gaze-related neurons. This is not in accordance at least with a simple and straightforward interpretation of gaze-related neurons carrying a spatial signal representing an earlier level in the visuomotor transformation than the gaze-independent neurons. Both facts argue rather in favor of the hypothesis that the gaze-related reach discharge is related to the time of actual movement execution.

Under natural reaching conditions, the gaze shift starts much sooner than the arm because of the different inertia of the eye (Biguer et al. 1982). Therefore the gaze axis already is oriented toward the reach target when the arm movement starts. A mismatch should be corrected quickly. There is good psychophysical evidence for the existence of a fast correcting mechanism during goal-directed arm movements in humans (Biguer et al. 1982; Goodale et al. 1986; Prablanc and Martin 1992). If during pointing, in some trials, the position of the target was suddenly shifted while the saccade toward the target reached its peak acceleration and the subjects just started the arm movement, they responded with a catch-up saccade directed toward the new target position. Because of saccadic suppression, the subjects were not aware of the perturbation. Nevertheless they also changed their ongoing arm trajectory so that the arm reach ended at the new location. This compensation took place with a latency of 150 ms. With a similar task, Alstermark et al. (1990) demonstrated for cats the same ability to switch on-line

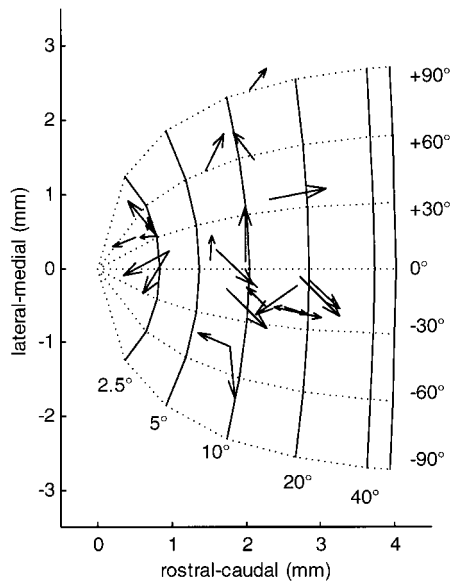

FIG. 12. Orientation of the RMFs for the 25 gaze-related reach neurons with respect to their location in the SC. Orientation of the RMF was calculated by the vector sum of the discharge measured during arm movements in the fixation reach task to the 4 locations orthogonally arranged around the fixation point. Length of the vector indicates the directional selectivity determined by projecting the activity amplitudes of the 4 reaching movements on to the calculated preferred direction vector. Although recordings were made from both superior colliculi (SC), all calculated directions are plotted with respect to the left SC. Therefore vectors pointing to the right indicate preferred reach targets in the visual hemifield contralateral to the recorded SC. Vectors pointing to the left indicate preferred reach targets in the visual hemifield ipsilateral to the recorded SC. All the vectors were plotted on a simplified oculomotor map of the SC (Ottes et al. 1986). Vector origin was placed at the coordinates of the visual receptive field measured in the same penetration while passing through the superficial layers.

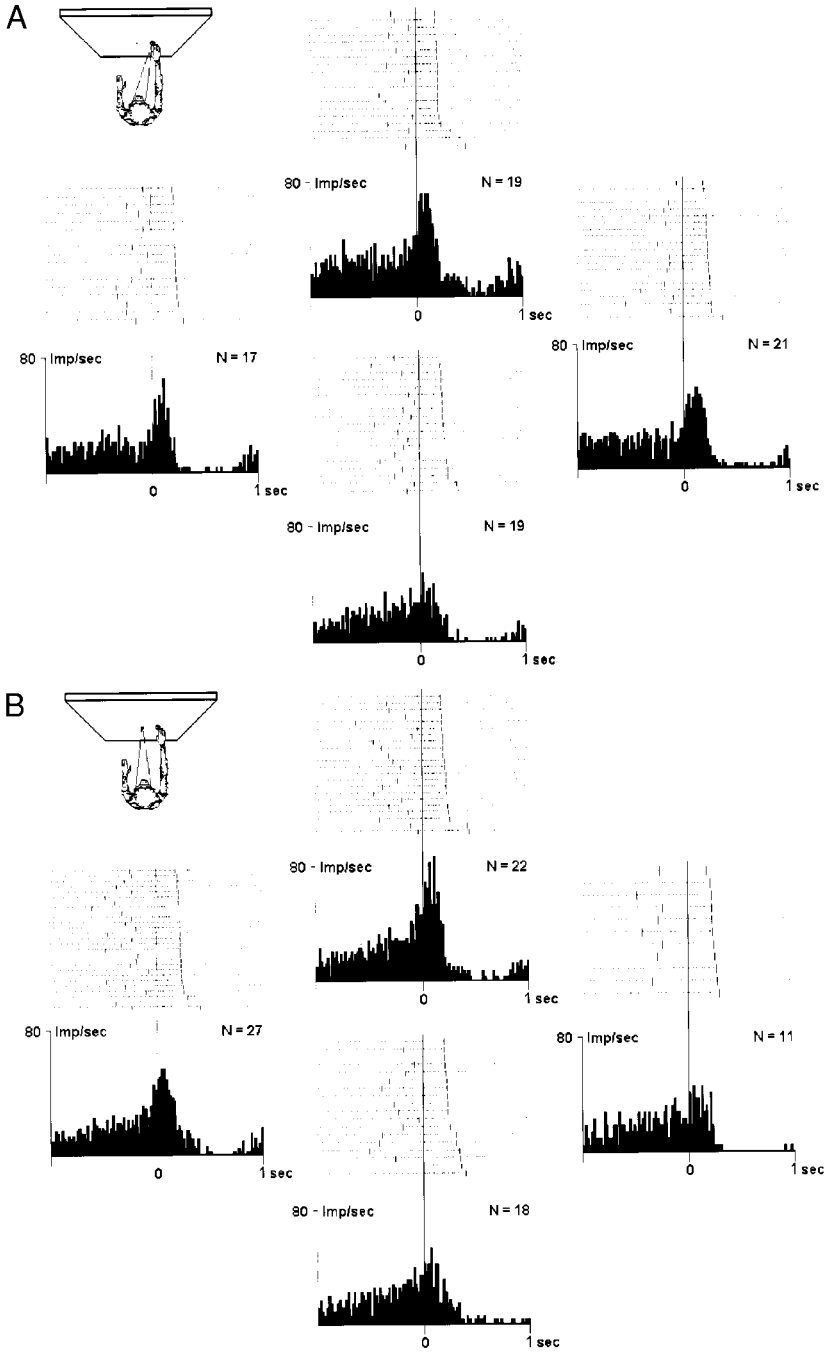

FIG. 13. Activity of a gaze-independent reach neuron. Cell was recorded in the left colliculus of *monkey C*. Activity of the neuron is displayed as raster plots and histograms (bin size, 20 ms). Data are aligned on the onset of the arm movement (vertical line at $t = 0$). Conventions as in Fig. 10. *A*: activity in the saccade reach task during 4 different targets each at a distance of 15° from the central fixation point. Location of the histograms indicate the position of the respective target. *B*: activity in the fixation reach task while the monkey reaches to the same 4 targets but keeps fixation of the central point. Note that response amplitudes and directional tuning of the neuron are identical irrespective of whether tested in the SR or FR task.

from one target to another with a latency of 80–120 ms. Transsection of the cortico- and rubro-spinal tract did not alter this ability. Interruption of the tecto-spinal and tecto-reticulo-spinal tracts on the other hand lead to a prolongation of the switch latency and an initial ataxia of the forelimb (Alstermark et al. 1987, 1990).

The SC might be the neural substrate involved in this automatic on-line correction mechanism for reaching movements also in primates. The activity of the gaze-related reach neurons signals the amplitude and direction of the difference between the targets of the two control systems for gaze and reach. This measure of gaze-arm-orientation mismatch provides a motor-error signal about the relative change in the arm movement trajectory that is necessary to get to the fixated target. But there are also situations requiring the dissociation of the targets for attention, gaze, and arm movement. An example of such a situation is the FR task used in our study. The premotor cortex (PM) is discussed for its role in mediating arbitrary visuomotor transformations (Wise et al. 1997). To do this, PM and more generally also other parts of the frontal cortex have to learn the arbitrary mapping rules and execute them if needed. But in such a situation the cortex also would have to cancel the motor control commands coming from other parts of the brain that result from the standard visuomotor mapping rules. Therefore in a normal primate the cortex controls the SC and the rest of the brain stem (Dias et al. 1995; Pierrot-Deseilligny et al. 1991; Schlag-Rey et al. 1992; Segraves and Goldberg 1987). In this context, it is interesting to note the results of the ablation of

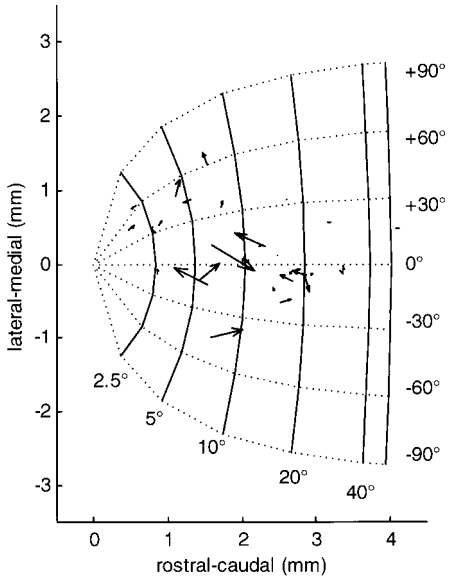

FIG. 14. Orientation of the RMFs for the 40 gaze-independent reach neurons with respect to their location in the superior colliculus (SC). RMF orientation and the location of the vectors on the map were examined in the same way as for Fig. 10. Vectors to the right indicate preferred reach targets in the hemifield contralateral to the SC, vectors pointing to the left indicate preferred reach targets in the hemifield ipsilateral to the SC recorded. Note the short length (weaker directional tuning) of the vectors in comparison to the vectors shown in Fig. 12.

PM, frontal eye field (FEF), and supplementary eye field (SEF) in the rhesus monkey (Moll and Kuypers 1977). This lesion leaves the ability for standard reaching intact but specifically results in an inability to unlock the targets for the eyes and the hand in a test of detour reaching. This compulsion of the arm to reach straight to a fixated visual target is exactly what is to be expected if the proposed collicular servomechanism dictates the reach because the ablated cortical areas cannot exert their inhibitory control on the SC any more.

Visual attention

Primates are able to attend to peripheral objects while maintaining eye fixation, i.e., without an overt gaze shift to the attended location (Corbetta et al. 1998). Such a covert shift of spatial attention leads to activity changes in build-up neurons in the SC, although no saccade will be executed (Kustov and Robinson 1996). A redirection of attention without a saccade is also necessary during the performance of the FR task. One might ask if the gaze-related reach activity really was related to the arm movement or whether it is just the result of an intended but not executed gaze shift or shift of attention to the location of the reach target in the FR task. A couple of reasons make the covert gaze shift hypothesis very unlikely. Only a minority of gaze-related neurons (2/25) is active before and during saccades without arm movement. The activity of almost all of the reach neurons starts before arm movement onset and not with target onset (see Fig. 15). Finally the RMF of nearly half of the gaze-related reach neurons is directed into the ipsilateral visual hemifield. This activity could hardly be interpreted as subliminal oculomotor activity in the SC because to our knowledge saccade-related neurons whose saccadic movement field is oriented in such a way have never been described in three decades of extensive research in this structure. It is unclear, however, whether a system responsible for the shift of visual attention has to conform to the saccadic system or can be active in a broader range of circumstances. We could imagine that in our FR task activity of gaze-dependent reach cells could be used to shift spatial attention to where the hand is going only with the onset of the actual execution of the reach.

Does the activity of gaze-dependent reach neurons represent an efference copy? This possibility is difficult to be ruled out at any level in the sensorimotor system. The SC neurons are only active if there is a certain spatial relationship between gaze axis and reach target. This fact argues against the interpretation as efference copy at least in its most simple version. A copy of the motor command should be present whenever there is a certain arm movement.

Comparison with other studies

Reach-related neurons that operate in a gaze-centered coordinate system exist both in the parietal and frontal cortex. Recently an area in the posterior parietal cortex (PPC) overlapping with areas V6A and medial intraparietal area has been described to contain neurons specialized for the planning of reach movements (Snyder et al. 1998). It has been found that the neurons in this area code in eye-centered coordinates (Batista et al. 1999). These cells show a remarkable similarity with the gaze-related reach neurons presented in this study except for the timing of their neuronal discharge. Whereas the onset of activity of most collicular cells is only with the beginning of motor execution, the parietal cells begin to discharge shortly after the target presentation. This suggests a difference in function. The posterior parietal cortex probably is involved in early stages of motor planing and attentional processes related to target selection. It also might supply the superior colliculus with information about the position of the reach target with respect to the gaze axis. Desmurget et al. (1999) showed in humans that transcranial magnetic stimulation of the PPC disrupted path correction of pointing movements in the dark to visual targets that had been moved during saccadic eye movements. They interpreted their results as evidence for a role of the PPC in a feedback loop that adjusts on-line the muscle activation pattern. The PPC might in part put the gaze-related reach neurons of the SC in the loop to influence the motor machinery. The other important target of the parietal cortex is the frontal cortex, especially the PM. This cortical area is involved in the planing and execution of limb movements (Boussaoud 1995; Wise et al. 1997) and projects to the motor cortex, to the basal ganglia as well as directly to the spinal cord (He et al. 1993). The gaze-modulated neurons in PMv described by Mushiake et al. (1997) show the most compelling similarities to the gaze-dependent reach neurons in the SC. Like their collicular counterparts, the PMv neurons operate in a gaze-related coordinate frame, and they are active in relation to the execution of reaching movements. Both the posterior parietal cortex and the mentioned frontal areas (PM, SEF, FEF) project to the superior colliculus and the underlying mesencephalic reticular formation (Fries 1984, 1985; Huerta and Kaas 1990). Therefore these cortical areas together with

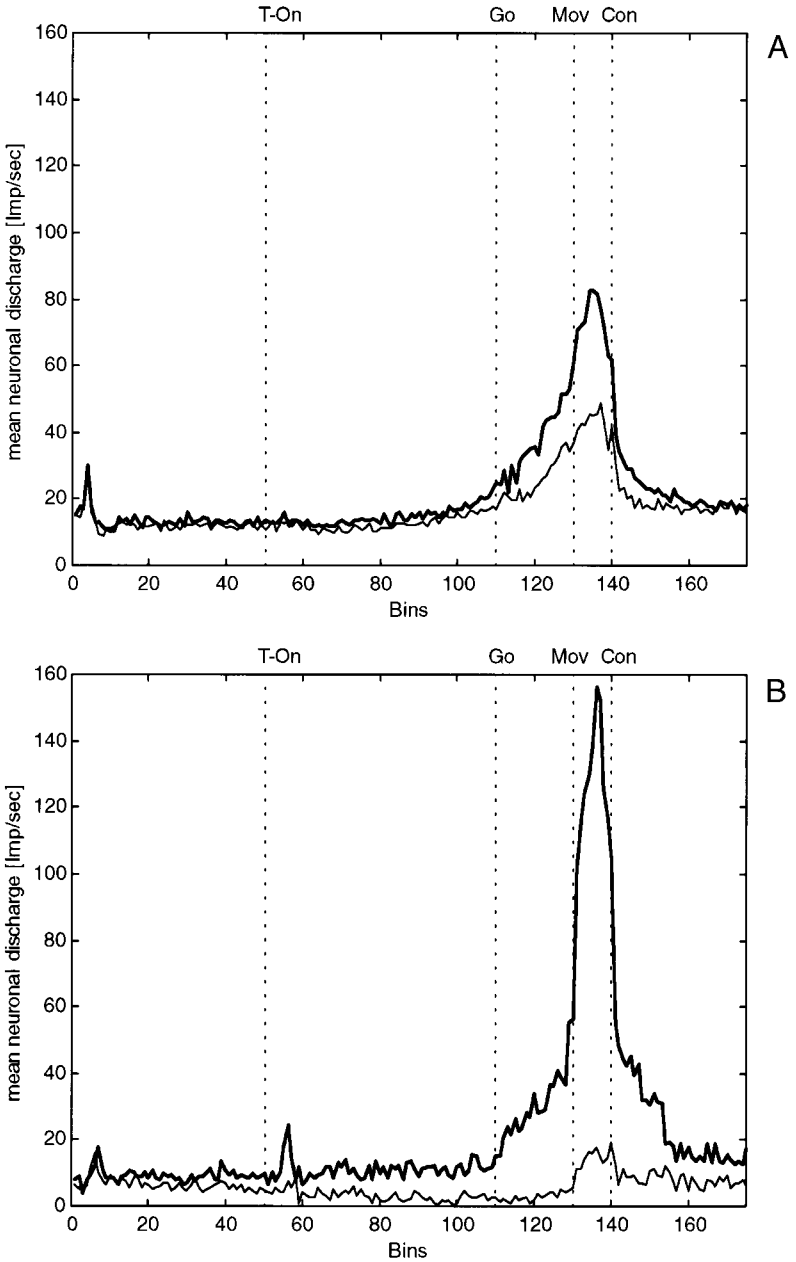

FIG. 15. Relative time histograms of the average discharge of the 2 populations of reach neurons in the FR task. *A*: mean neuronal discharges of the gaze-independent reach cells. Bold line gives the activity of the population during reach to the most preferred target, whereas the thin line gives the activity of the population during reach to the least preferred target. Vertical dashed lines mark the succeeding events: target-onset (T-On), GO signal (Go), arm movement onset (Mov), and contact (Con) with the reach target. *B*: mean neuronal discharges of the gaze-dependent reach cells. Note the weaker modulation but the earlier beginning of the rise in the average population activity for the gaze-independent population shown in *A*. For calculation of the relative time histogram, see METHODS.

the midbrain might form a closely integrated network devoted to the coordination of eye and arm movements.

Conclusions

Besides the well-known sensorimotor neurons that shift the gaze toward a target (Munoz and Wurtz 1995), two new populations of neurons have been described in this paper that are active before and during arm movements. The first population located exclusively in the SC operates in a gaze-related coordinate system. These cells might carry signals representing the goal for the arm movement in a gaze-centered reference frame or they might represent a motor error signal used by a servosystem for steering of the hand toward the point in space the monkey is fixating. In either case, their reference system is suited ideally to use the sensory information provided by visual, auditory, and somatosensory cells in the SC, all operating also in a gaze-related reference frame (Jay and Sparks 1984; Mays and Sparks 1980). The discharge of the second population that is located deeper in the SC and in the underlying MRF is related more directly to the actual movement and operates in a gaze-independent reference frame.

At the moment no direct evidence exists about the anatomic connection of the two classes of reach cells. The majority of descending tectofugal axons arise from collicular laminae that lie ventral to the stratum opticum. Such descending axons can be grouped into two major bundles or tracts, i.e., the ipsilateral tectopontine-tectobulbar tract and the crossed tectospinal tract (or the predorsal bundle). The ipsilateral pathway projects among other targets to the mesencephalic reticular formation and the cuneiform nucleus (Harting 1977). The tectospinal

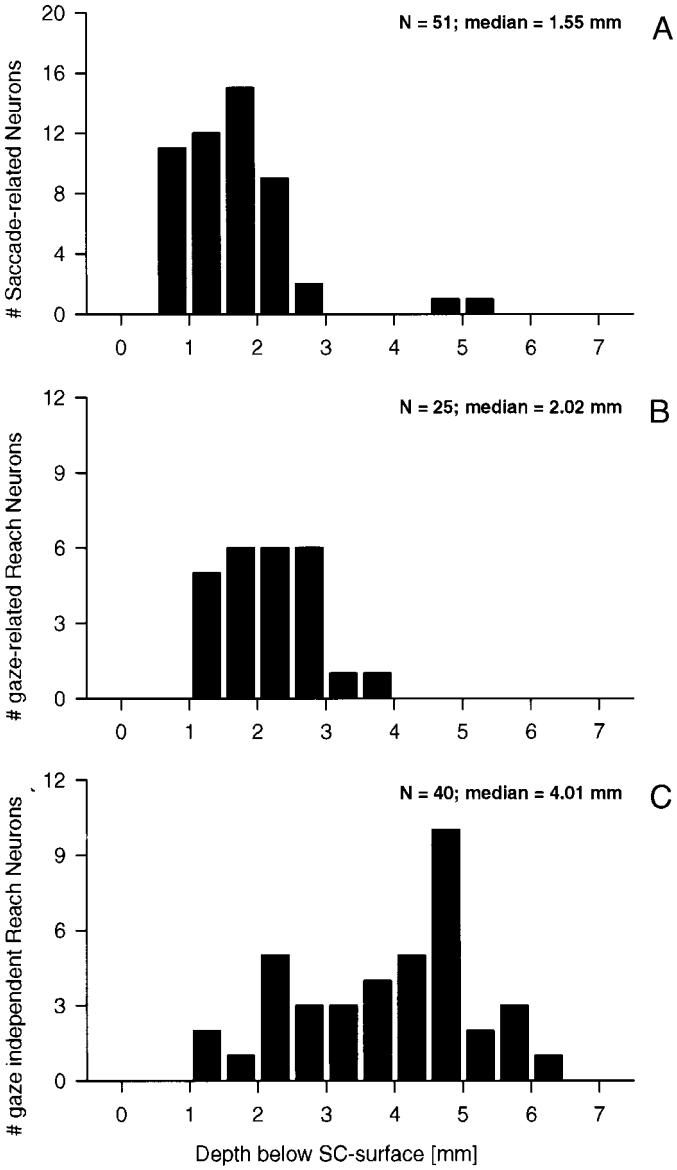

FIG. 16. Recording depth of saccade-related neurons (*A*), gaze-related reach neurons (*B*), and gaze-independent reach neurons (*C*) below the surface of the SC. Median depth of the gaze-related cells and the saccade cells encountered in the same recording sessions are 1.55 and 2.02 mm, respectively, whereas most of the gaze-independent reach cells were recorded in the deeper layers of the SC as well as in the underlying reticular formation. They have a median depth of 3.85 mm below the SC surface. A Kruskal-Wallace test ($P > 0.05$) showed that there was no significant difference between the depth distribution of saccade-related and gaze-related reach neurons, whereas the depth distribution of the gaze-independent neurons was significantly different from the 2 others.

tract belongs together with the reticulospinal tract to the ventromedial descending brain stem system (Lawrence and Kuypers 1968). The combined projections of this system terminate within parts of the spinal cord that innervate axial and proximal arm muscles. The discharge of some of the gaze-independent reach neurons is correlated highly with the activity of muscles from the shoulder girdle and the upper arm (Stuphorn et al. 1999; Werner et al. 1997a). Others are related to the end point or the direction of the arm movement (Stuphorn et al. 1995). These findings fit well to a picture of the SC as a brain structure mainly involved with the spatial orientation of different body parts like reaching toward a point in external space but not with the fine control of the hand and fingers necessary for grasping and manipulating objects. The connection between SC and spinal cord in primates is probably not via direct projections to a C_3–C_4 propriospinal system (Maier et al. 1998). Instead it might be an indirect connection via arm-reaching related neurons further caudal in the brain stem (Ruffo and Buford 1997).

Another possible target for the reach-related neurons in the colliculus might be the cerebellum via the ipsilateral tectopontine projection. It recently has been shown that Purkinje cells encode both destination and error (i.e., deviation of the final arm position from the intended one) of arm movements (Kitazawa et al. 1998). This information that is represented in the discharge of collicular reach neurons could possibly be of great importance for the cerebellum to contribute to the long-term improvement of movements (Gilbert and Thach 1977; Houk et al. 1996). In any case, our results further add to the hypothesis that neurons in the SC and the underlying MRF are integrated in the neuronal network controlling arm movements in primates.

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