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RESEARCH ARTICLE

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Predictive responses of periarcuate pursuit neurons to visual target motion

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Abstract The smooth pursuit eye movement system uses retinal information about the image-slip-velocity of the target in order to match the eye-velocity-in-space (i.e., gaze-velocity) to the actual target velocity. To maintain the target image on the fovea during smooth gaze tracking, and to compensate for the long delays involved in processing visual motion information and/or eye velocity commands, the pursuit system must use prediction. We have shown recently that both retinal image-slip-velocity and gaze-velocity signals are coded in the discharge of single pursuit-related neurons in the simian periarcuate cortex. To understand how periarcuate pursuit neurons are involved in predictive smooth pursuit, we examined the discharge characteristics of these neurons in trained Japanese macaques. When a stationary target abruptly moved sinusoidally along the preferred direction at 0.5 Hz, the response delays of pursuit cells seen at the onset of target motion were compensated in succeeding cycles. The monkeys were also required to continue smooth pursuit of a sinusoidally moving target while it was blanked for about half of a cycle at 0.5 Hz. This blanking was applied before cell activity normally increased and before the target changed direction. Normalized mean gain of the cells' responses (re control value without blanking) decreased to 0.81(±0.67 SD), whereas normalized mean gain of the eye movement (eye gain) decreased to 0.65 (±0.16 SD). A majority (75%) of pursuit neurons discharged appropriately up to 500 ms after target blanking even though eye velocity decreased sharply, suggesting a dissociation of the activity of those pursuit neurons and eye velocity. To examine whether pursuit cell responses contain a predictive component that anticipates visual input, the monkeys were required to fixate a stationary target while a second test laser spot was moved sinusoidally. A majority (68%) of pursuit cells tested responded to the second target motion. When the second spot moved abruptly along the preferred direction, the response delays clearly seen at the onset of sinusoidal target motion were compensated in succeeding cycles. Blanking (400–600 ms) was also applied during sinusoidal motion at 1 Hz before the test spot changed its direction and before pursuit neurons normally increased their activity. Preferred directions were similar to those calculated for target motion (normalized mean gain=0.72). Similar responses were also evoked even if the second spot was flashed as it moved. Since the monkeys fixated the stationary spot well, such flashed stimuli should not induce significant retinal slip. These results taken together suggest that the prediction-related activity of periarcuate pursuit neurons contains extracted visual components that reflect direction and speed of the reconstructed target image, signals sufficient for estimating target motion. We suggest that many periarcuate pursuit neurons convey this information to generate appropriate smooth pursuit eye movements.

Keywords Smooth pursuit · Prediction · Periarcuate cortex · Frontal eye fields · Visual motion

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Introduction

With the development of the high acuity fovea in primates, smooth pursuit eye movements have evolved to track an interesting object that moves slowly across the visual field. The smooth pursuit system uses retinal image-slip-velocity information of the target to match the eye-velocity-in-space (i.e., gaze-velocity) to the actual target velocity that is required to maintain the target im-

age on the fovea during smooth gaze tracking (for reviews, see Robinson 1981; Leigh and Zee 1999). To compensate for the long delays involved in processing visual motion information and/or eye velocity commands, the pursuit system must use prediction and is quite efficient, especially when target movement is periodic (Becker and Fuchs 1985; Barnes 1993; Kettner et al. 1996). However, predictive mechanisms underlying smooth pursuit are still incompletely understood (see, for example, Suh et al. 2000). To explain known pursuit characteristics, Robinson (1982) extended Young's internal positive feedback model (see, for example, Yasui and Young 1975) and proposed a model in which the pursuit system uses an internal representation of target velocity derived from retinal image-slip-velocity of the target and an efference copy of eye velocity and head velocity (see also Robinson et al. 1986). The model (Robinson 1982) explains many characteristics of smooth pursuit eye movements including prediction of target velocity. However, the fundamental question of where such an estimate of target velocity actually manifests has not been clearly answered (cf. Robinson et al. 1986; Suh et al. 2000).

The medial superior temporal (MST) area is essential for initiation and maintenance of smooth pursuit (for reviews, see Lisberger et al. 1987; Andersen et al. 1997; Leigh and Zee 1999; also Dürsteler and Wurtz 1988; Dicke and Thier 1999). The MST area contains all the signal components needed to reconstruct target motion in space including retinal image-slip-velocity, eye velocity, and even gaze-velocity (Sakata et al. 1983; Kawano et al. 1984; Komatsu and Wurtz 1988a, c; Newsome et al. 1988; Thier and Erickson 1992; see Andersen et al. 1997 for review). Moreover, since the discharge of pursuit cells in the MST area is maintained even when the actual target is briefly extinguished, it has been suggested that this area forms an internal positive feedback circuit in the pursuit system for the maintenance of pursuit (Newsome et al. 1988). However, since the origin of the eye velocity signals in the MST area is still unknown (Andersen et al. 1999), it is still not clear how the MST area could be involved in the internal positive feedback circuit for the maintenance of pursuit or in an estimating target velocity.

Parts of the frontal eye fields (FEF), particularly in the fundus and posterior bank of the arcuate sulcus, are also thought to be involved in smooth pursuit (Bruce and Goldberg 1985; Bruce et al. 1985; Lynch 1987; Keating 1991, 1993; MacAvoy et al. 1991; Gottlieb et al. 1993, 1994; Tian and Lynch 1996a, b; Tanaka and Fukushima 1998; Fukushima et al. 2000a; Tanaka and Lisberger 2001). The majority of such periarcuate pursuit neurons also carry signals related to eye velocity, gaze-velocity, and even retinal image-slip-velocity (MacAvoy et al. 1991; Gottlieb et al. 1994; Tanaka and Fukushima 1998; Fukushima et al. 2000a), similar to MST pursuit neurons. Moreover, since surgical ablations and chemical inactivation of the periarcuate pursuit areas impair smooth pursuit and smooth gaze tracking during whole body rotation (Lynch 1987; Keating 1991; MacAvoy et al. 1991; Shi et al. 1998; Fukushima et al. 1999a), periarcuate pursuit neurons seem to be positioned to issue eye- and gaze-velocity commands (Tanaka and Fukushima 1998; Fukushima et al. 2000a). MacAvoy et al. (1991) reported that surgical ablations of these areas produce substantial deficits in the anticipatory initiation and predictive continuation of smooth pursuit, although this conclusion remains somewhat controversial (Keating 1991, 1993).

Prediction in smooth pursuit could occur in different ways. It could occur not only on the motor side as preparation for and maintenance of ongoing movements, but also on the sensory and/or perception side as, for example, a visual response that anticipates the eventually renewed visual target input (cf. Umeno and Goldberg 1997) about the direction and speed of the target movement. To understand whether periarcuate pursuit neurons play a role in predictive smooth pursuit, we asked three main questions in this study. First, using a sinusoidal smooth pursuit task, we examined whether the long delays involved in processing of the above signals are compensated at the level of periarcuate pursuit neurons. Second, we asked how cell activity is correlated with predictive eye movements by extinguishing a tracking target (cf. Becker and Fuchs 1985). This blanking was applied before a sinusoidally moving target changed its direction. The monkeys were required to continue their pursuit by changing direction without the presence of a target. Although we have qualitative observations under these conditions (Fukushima et al. 2000a), we quantified here cell activity and eye velocity when the tracking target was extinguished for almost half a cycle. Third, to test whether periarcuate pursuit neurons carry predictive visual signals about the direction and speed of the target movement, we examined their activity during a fixation task while a second laser spot moved sinusoidally. We asked whether these cells respond to the second target motion even when the actual retinal target-motion is eliminated by extinguishing the moving test spot for almost half of each cycle. We will show that the majority of periarcuate pursuit neurons indeed carry predictive signals. Some of these results have been presented in preliminary form (Fukushima et al. 2000b).

Materials and methods

Methods

Four male Japanese monkeys (*Macaca fuscata*, N, C, T, H; 4.5–6.0 kg) were used. All procedures were evaluated and approved by the Animal Care and Use Committee of the Hokkaido University School of Medicine (protocol number 9290). Our methods for animal preparation and training are described in detail elsewhere (Fukushima et al. 1999b, 2000a). Briefly, each monkey was sedated with ketamine hydrochloride (5 mg/kg, i.m.), and then anesthetized with Nembutal (25 mg/kg, i.p.). Under aseptic conditions, head-holders were installed to restrain the head firmly in the primate chair in the stereotaxic coordinates during recording sessions and a scleral search coil was implanted on the right eye to record vertical and horizontal components of eye movement (Fuchs and Robinson 1966; Judge et al. 1980). Analgesics and antibiotics were administered postsurgically to reduce pain and pre-

vent infection. Following a week of recovery, the monkeys were trained for apple juice reward to track a laser spot (0.2° in diameter) that was back-projected onto a tangent screen in an otherwise completely dark room.

Recordings were made in the periarcuate cortex at Ant. 21–27 and Lat. 10–15 stereotaxic coordinates as previously described (Tanaka and Fukushima 1998; Fukushima et al. 2000a). All stimuli were applied sinusoidally. Single neurons responding to smooth pursuit were located and pursuit responses were tested in four planes (vertical, horizontal, and two oblique directions at 45° and 135° polar angle) at 0.5 Hz (±5 or 10°) to determine the preferred direction for pursuit activation of each cell. A target was moved abruptly along different directions for several cycles to examine initial tracking responses (see Results). As in previous studies (see, for example, Gottlieb et al. 1994), pursuit-related neurons with preferred directions are called pursuit cells in this study. During continuous sinusoidal tracking in the preferred direction, the target was extinguished (blanked) for 800–1,000 ms shortly before it changed direction at a fixed position in each cycle at 0.5–0.7 Hz (±10°). Blanking was timed so it occurred before the pursuit neuron would have normally increased its activity. The monkeys were required to continue pursuit by changing tracking velocity and direction without the aid of the target.

In the second task, visual responses of pursuit neurons were examined by requiring the monkeys to fixate a stationary laser spot (fixation spot, 0.2° in diameter) while a second laser spot (0.6° in diameter) moved sinusoidally along one of the four directions at 1.0 Hz (±10°). The fixation spot was extinguished periodically while the second test spot was presented continuously. Extinction of the fixation spot cued the monkeys to track the second moving spot. This procedure was used to reward the monkeys for pursuing the second spot so that it would not become behaviorally meaningless and so that the monkeys attended to it. We then examined the response to the second spot by extinguishing it for about half of each cycle (400–600 ms, at 1 Hz) while the monkeys fixated the first stationary spot. Blanking was applied at a fixed position in a cycle, before the second spot changed direction, and was timed so it occurred before pursuit cells increased their activity to the second spot. In both tasks, target blanking was given as a block of 15–20 cycles followed by control cycles without blanking, and this sequence was repeated a few times for each direction for each neuron.

To examine whether retinal slip information is necessary for the visual response of our cells, we presented the test spot sequentially (flash rate at 20 or 30 Hz, duration of each flash 15 or 25 ms, flash-to-flash distance 0.7–1.0°) as it moved sinusoidally at 0.5 Hz (±10°) while the monkeys fixated a stationary spot. Such "apparent motion stimuli" should simulate target velocities of approximately 14–30°/s (=0.7°/50 ms to 1°/33 ms; Churchland and Lisberger 2000). We used such stimuli to examine qualitatively whether the retinal image-motion-response of pursuit neurons requires actual retinal image-slip of the second spot but not to perform quantitative analysis. To avoid any visible streak during the flash, the laser spot was extinguished while it jumped and was turned on only when its position was stationary (Tanaka and Fukushima 1998). The animals were rewarded for fixating the first stationary spot. Since neither the eyes nor the test spot were moving, this paradigm should not create retinal slip of the target image (Mikami et al. 1986; Mikami 1992). Typically 15–20 trials were run for each task condition. Blanking was tested in non-preferred directions as well.

Data analysis

The data were analyzed off-line as previously described (Fukushima et al. 1999b, 2000a). Cell discharge was discriminated with a dual time-amplitude-window discriminator and digitized together with eye position and target position signals at 500 Hz using a 16-bit A/D board. Position signals were differentiated to obtain velocity by analog circuits (DC-50 Hz, –12 dB/octave) which were low-pass filtered (30 Hz, –6 dB/octave). Saccades were marked on eye velocity traces using a cursor and were removed using an interactive computer program. Initial tracking response was analyzed by visual inspection. We analyzed only those cells that showed clear peak discharges in response to target velocity (see Results). Blanking effects were analyzed by averaging over 10–20 cycles of eye velocity, stimulus velocity and firing rates. For the cell-response, each cycle was divided into 64 equal bins. These traces were then averaged to obtain mean velocities, rasters, and histograms of discharge for each session. In the second task, traces that contained saccades or slow eye movement were removed since they were indicative of the monkeys' failure to fixate the stationary spot, and only those traces with eye position changes of less than 1° during each cycle were analyzed.

To quantify responses, a sine function was fitted to the cycle histograms of cell discharge, exclusive of the bins with zero spike rate, by means of a least-squared error algorithm. Responses that had a harmonic distortion (HD) of more than 50% or a signal-to-noise ratio (S/N) of less than 1.0 were discarded. The S/N was defined as the ratio of the amplitude of the fitted fundamental frequency to the root mean square amplitude of the third through eighth harmonics and HD as the ratio of the amplitude of the second harmonic to that of the fundamental (Wilson et al. 1984). The phase shift of the peak of the fitted-function relative to upward or rightward stimulus velocity was calculated as a difference in degrees. Gain was calculated as the peak amplitude of the fundamental component fitted to the cycle histogram divided by the peak amplitude of the fitted stimulus velocity. Gain ≥0.10 spikes/s per °/s was taken as significant modulation. For responses with oblique preferred directions, radial stimulus velocity was first calculated as the square root of the sum of the squares of the vertical and horizontal components, and gain was calculated by dividing amplitude of modulation by radial stimulus velocity. Eye velocity responses were calculated similarly after deleting saccades. The preferred activation direction of each cell was estimated by the method of Krauzlis and Lisberger (1996) using a Gaussian function as previously described (Fukushima et al. 2000a). Discharge rate of each cell during straight-ahead gaze before the first series began was used as the resting rate.

The locations of recording sites in three monkeys were histologically verified as in previous studies (Tanaka and Fukushima 1998; Fukushima et al. 2000a). The fourth monkey (H) is still being used for other experiments, but discharge characteristics of pursuit cells in this monkey were similar to those of our previous studies, so we are certain that recordings in the monkey H also were from the similar regions.

Results

In this study we analyzed responses of a total of 116 periarcuate pursuit neurons (see Methods) in four monkeys. These include 8 cells from monkey N, 44 cells from monkey C, 57 cells from monkey T, and 7 cells from monkey H. We will first describe discharge characteristics associated with predictive tracking eye movements.

Discharge of periarcuate pursuit neurons during predictive smooth pursuit eye movements

Response during initial sinusoidal tracking

As described above, the pursuit system must use prediction to compensate for the long delays involved in processing visual motion information and/or eye velocity commands. We first asked whether such delays are compensated at the level of periarcuate pursuit neurons. Re-

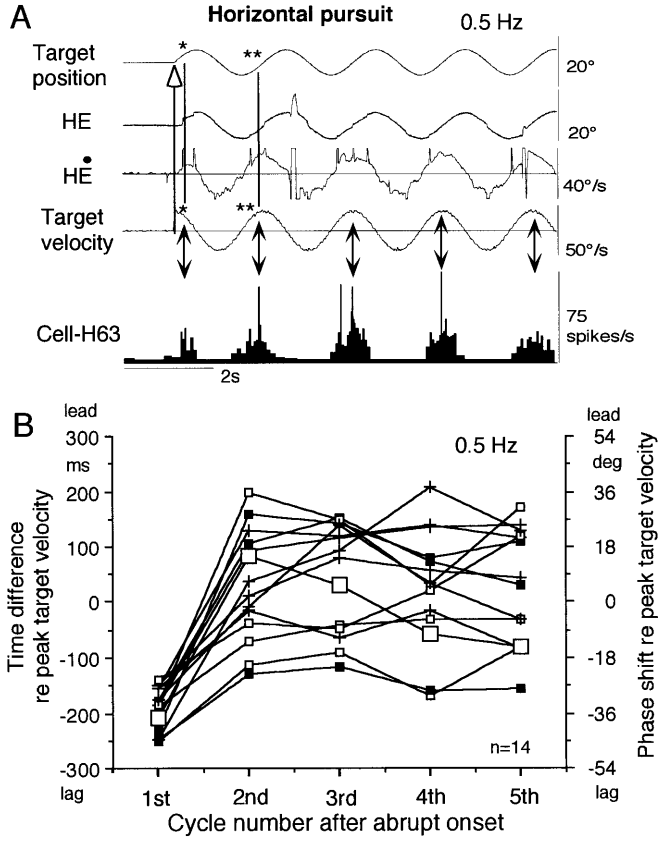

Fig. 1A, B Responses of periarcuate pursuit neurons during abrupt movement of a tracking target. **A** Discharge of a representative neuron. *Open arrow* Stationary target abruptly moved rightward. *Double-headed arrows* Peak discharge time of this cell is indicated for the first five consecutive cycles. *Single asterisks* and *straight line* Cell's peak discharge lags peak target velocity in the first cycle. *Double asterisks* and *straight line* Discharge delay is compensated in the second cycle. **B** Plots time difference between peak discharge and peak target velocity of 14 cells for the first five cycles of sinusoidal target motion at 0.5 Hz. Abrupt target motion was always applied along the preferred direction of each cell as in **A**. Responses of the same cells are connected by *lines*. The cell shown in **A** is plotted as *large open squares* in **B**. Cells that showed visual response are plotted with *filled squares*. Cells that did not show visual response are plotted with *open squares*. + Cells in which visual responses were not tested. HE and HE are horizontal eye position and velocity, respectively. Saccade velocities exceed the plotting scale in **A**

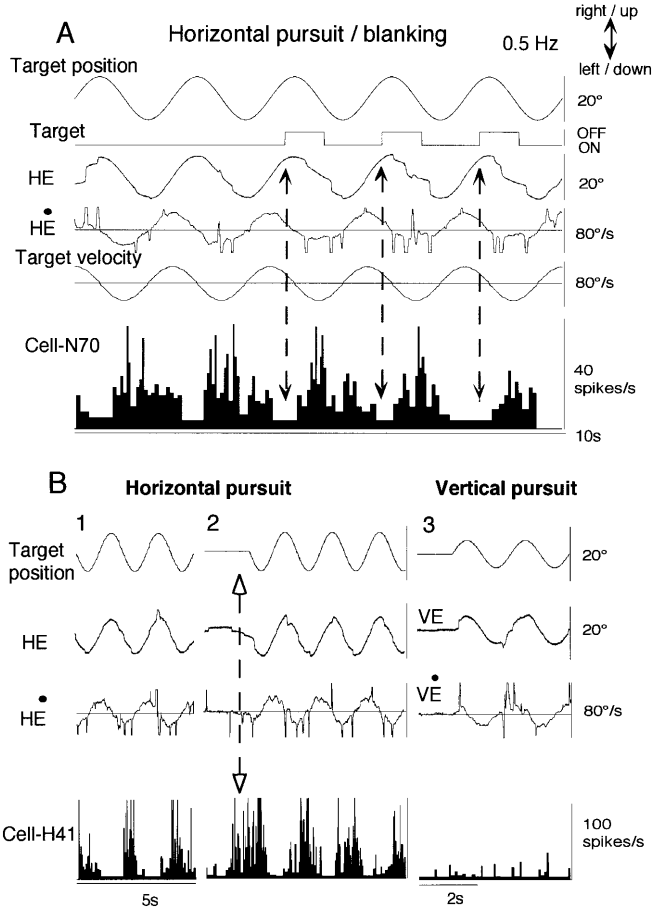

Fig. 2A, B Prediction-related activity of two different periarcuate pursuit neurons. **A** Comparison of responses when the tracking target was on and when it was extinguished during the periods indicated (*OFF*). *Double-headed arrows connected by a dashed line* Onset of blanking. **B** Responses of another neuron (**B***1*) at the beginning of predictable target motion when it was applied along the preferred direction (**B***2*) or along the non-preferred direction (**B***3*). *Open arrowheads connected by dashed line* Discharges before the target actually started moving and before appreciable eye movement appeared. HE, HE, VE, and VE are horizontal eye position and velocity and vertical eye position and velocity, respectively

sponse delays of our cells clearly seen at the onset of sinusoidal target motion along preferred directions were compensated in the succeeding cycles. Figure 1A shows representative discharge of a single cell. This cell responded in phase with rightward eye/target velocity during sinusoidal pursuit. When a stationary target was abruptly moved rightward (Fig. 1A *open arrow*), the cell's peak discharge lagged peak target velocity (*asterisks* on target position and velocity traces). This delay was compensated in the next cycle showing clearly that the cell discharged in phase with peak target velocity to the right (*double asterisks*).

To examine compensation of the response time delays, we plotted time difference (re peak target velocity) for 14 cells in Fig. 1B. The stationary target moved abruptly at 0.5 Hz along the preferred direction for each cell as illustrated in Fig. 1A, and the time difference between peak discharge and peak target velocity of the five consecutive cycles was manually calculated as shown in Fig. 1A (*double-headed arrows*). Response lag (re peak target velocity) is shown in Fig. 1B for each cell. The response delays clearly seen in the first cycle were compensated by the second cycle, indicating that one cycle is sufficient for establishing a predictable smooth pursuit trajectory. Of the 14 cells, 8 were tested for visual responses while the monkeys fixated a stationary spot in the second task condition as described below. Of these 8 cells, 3 showed visual response (Fig. 1B *filled squares*), while the remaining 5, including the cell shown in Fig. 1A, did not (Fig. 1B *open squares*). Their responses were similar, suggesting that delay compensation occurs

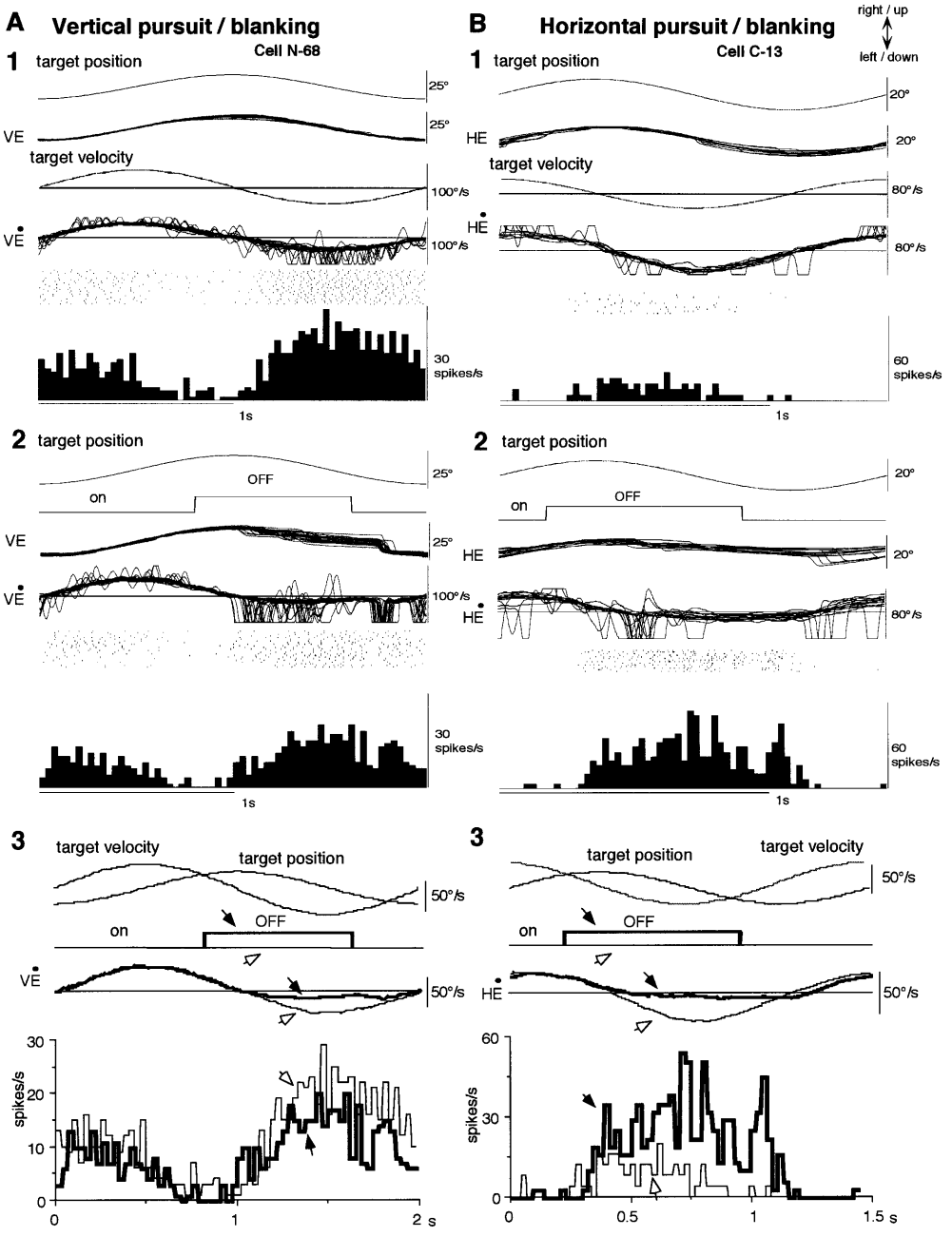

Fig. 3A, B Comparison of pursuit cell responses and tracking eye movements with and without target blanking. **A** and **B** are different cells. **A***1* and **B***1* are responses without blanking. Cell responses are illustrated with raster and histograms. **A***2* and **B***2* are responses with blanking (*OFF*). In **A***3* and **B***3* averaged eye velocities with (*thick lines*) and without blanking (*thin lines*) are superimposed together with spike histograms of the two cells. *Open arrows* Averaged eye velocity and cell discharge (*thin line*) when target was on. *Filled arrows* Averaged eye velocity and cell discharge (*thick line*) when target was blanked during the periods indicated (*OFF*). Abbreviations as in Fig. 2

in both visual and non-visual pursuit cells (see Discussion). Similar delay compensation was also observed when target frequency was abruptly changed.

Response during target blanking

Predictive responses related to perseverance of ongoing smooth pursuit eye movements are also clearly seen during target blanking when presented repeatedly in a block. This is illustrated in Fig. 2A for a different neuron with a horizontal preferred direction. After several cycles of sinusoidal tracking, the target was blanked just before the target and eye changed direction. This cell discharged clearly during target blanking associated with predictive eye movement along its preferred direction (i.e., leftward, Fig. 2A, *double-headed arrows* mark onset of blanking) but not along non-preferred directions (i.e., vertical, not shown).

The direction-specific predictive cell response is further illustrated in Fig. 2B. Its activity also seems to be related to preparation of smooth pursuit (Fig. 2B*1*). We repeated sinusoidal target presentation for several cycles at 0.5 Hz then stopped it for a few seconds. When this sequence was repeated a few times along the preferred direction, this cell discharged before the target actually started moving and before appreciable eye movement appeared (Fig. 2B*2* *open arrowheads connected by dashed line*). Such predictive discharge was not observed for the non-preferred direction (Fig. 2B*3*). This observa-

tion was confirmed in 12 other cells that also increased their discharge rate above the resting rate preceding the eye movement by 0–1.3 s with the mean of 0.38 s.

To further analyze predictive responses, we averaged cell discharge during target blanking (Fig. 2A) using raster histograms. Examples are illustrated in Fig. 3A, B for two neurons. Their activity is compared with the associated eye position and velocity during normal smooth pursuit (Fig. 3A*1*, B*1*) and with target blanking (Fig. 3A*2*, B*2*). In both neurons, blanking was applied before activity increased and before the target changed direction. Both monkeys performed the task by changing tracking direction in the complete absence of a visible target (Fig. 3A*2*, B*2*). Comparison of averaged cell discharge and eye velocity (Fig. 3A*3*, B*3*) with (*thick lines*) and without (*thin lines*) target blanking indicates that eye velocities remained unchanged for ca 0.2 s (Fig. 3B*3*) or ca 0.3 s (Fig. 3A*3*) after blanking the target, and then decreased. The discharge of the cell shown in Fig. 3A (*bottom*) decreased slightly, whereas the other cell (Fig. 3B) increased during target blanking despite consistent decrease in eye velocity.

A total of 24 pursuit neurons was examined in two monkeys during smooth pursuit at 0.5 Hz (±10°) with 800 ms blanking. Of these, 10 cells were tested by applying target blanking at least 150 ms before the cells normally increased their activity as illustrated in Figs. 2A and 3 (8 cells from monkey C, 2 cells from monkey N). In the remaining 14 cells (7 cells from monkey C, 7 cells from monkey N), blanking was applied almost simultaneously with the normal increase in discharge. The results obtained in these two groups of cells ("before" and "during", respectively) were analyzed separately and are summarized in Fig. 4. The change in discharge rate for the blanking period was estimated by the gain values that were calculated by fitting a sinusoid (see Methods) and is summarized in Fig. 4A, B. Results obtained in the two groups were similar. Mean (±SD) discharge changed from 0.44 (±0.31) to 0.36 (±0.21) spikes/s per °/s and from 0.55 (±0.46) to 0.29 (±0.37) spikes/s per °/s for "before" and "during" groups, respectively (Fig. 4C). Simultaneously recorded eye gains (see Methods) changed from 0.87 (±0.13) to 0.53 (±0.15) and from 0.94 (±0.05) to 0.64 (±0.14) for the two groups (Fig. 4D). Normalized gain values (re control value without blanking) are plotted in Fig. 4E, F for the two groups. The majority of them showed a decrease during target blanking with the normalized means (±SD) of 0.83 (±0.31, n=9; Fig. 4E) and 0.64 (±0.53, n=14; Fig. 4F) of the control value without blanking for the "before" and "during" groups, respectively, whereas overall normalized eye gain decreased to 0.65 (±0.16). Thus, in both groups gain decrease was associated with eye gain decrease during blanking, and normalized overall mean gain for 24 cells was 0.81 (±0.67).

To make the blanking effects more clear, we calculated the difference in discharge rate with and without blanking. Discharge rate without blanking was subtracted from discharge rate with blanking for each cell, and

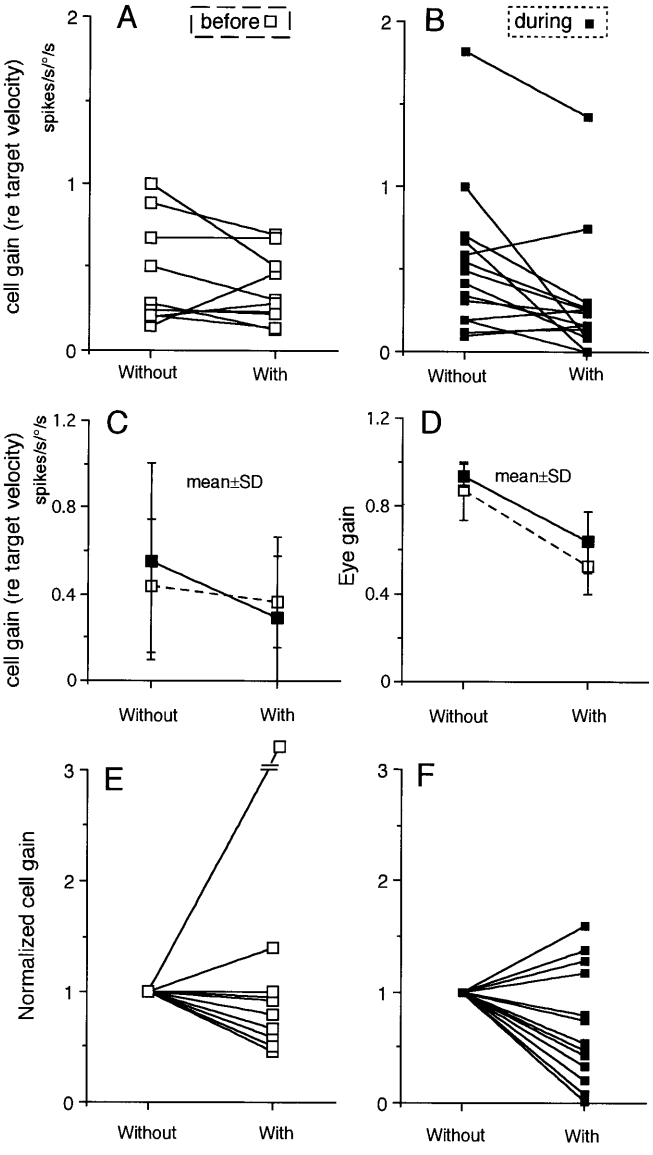

Fig. 4A–F Comparison of pursuit cell gains (re target velocity) with and without blanking of a tracking target. **A**, **B** Plot gains of individual cells. *Open squares* show gains when target blanking was applied more than 150 ms before these cells increased activity ("before"). *Filled squares* show gains when target blanking was applied almost simultaneously with the onset of discharge ("during"). Cells shown in **A** and **B** are different. Values of the same cells are connected by *lines*. **C** Mean (±SD) gains for the two groups of cells. **D** Eye gains for the two groups of cells. **E**, **F** Normalized gains for the "before" and "during" groups of cells, respectively

the differences were plotted for the two groups (Fig. 4A, B) aligned on the blanking onset in Fig. 5A, B. These panels show that the differences in discharge rates of individual cells varied but that their differences scattered mostly around zero before the target was extinguished (Fig. 5A, B). After blanking the target, discharge rate differences of the majority (18/24=75%) of them still scattered around zero, and only six cells exceeded the maximal difference before the target was extin-

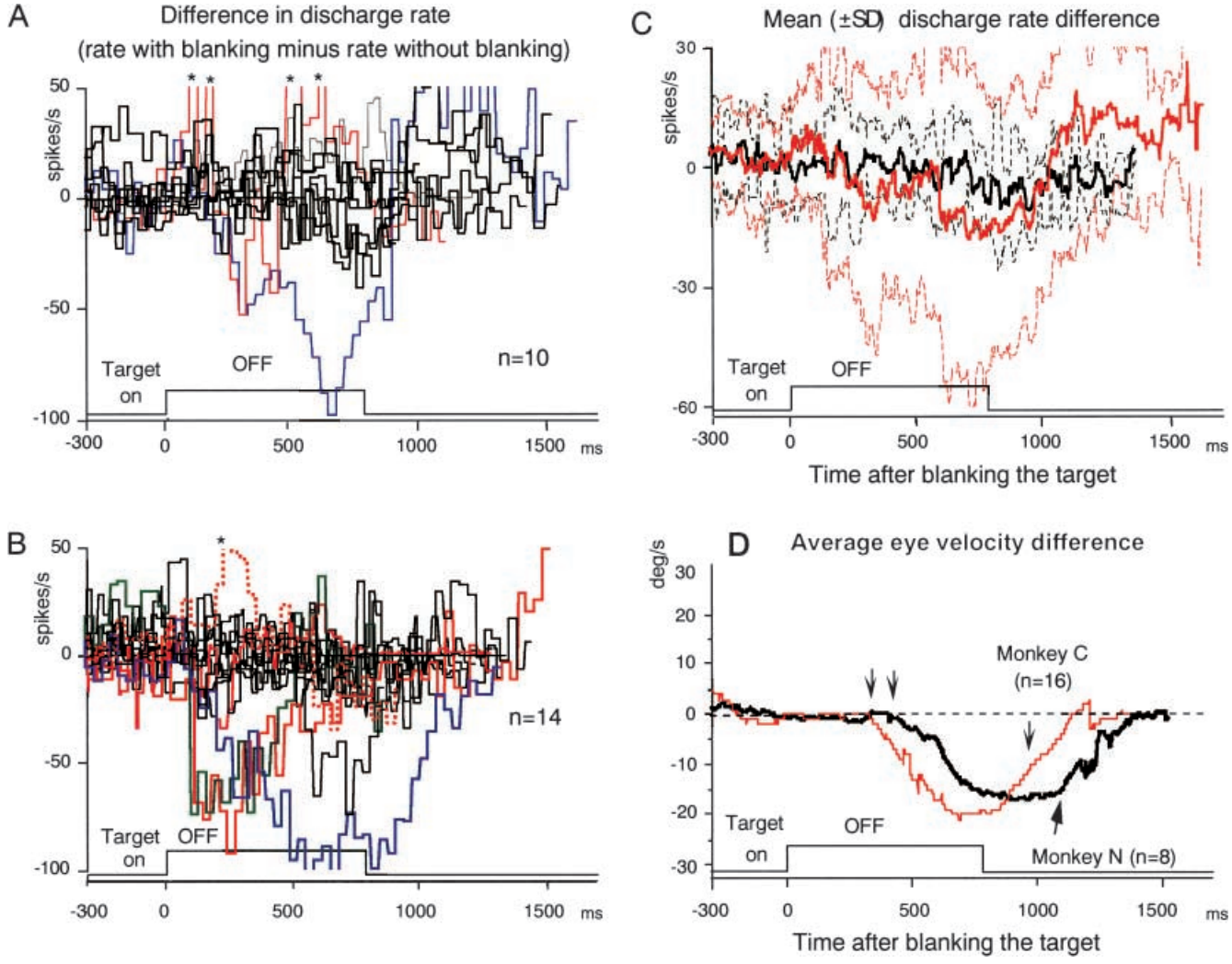

Fig. 5A–D Differences in discharge rates of periarcuate pursuit cells with and without blanking of the tracking target. Discharge rate without blanking was subtracted from that with blanking for each cell (n=24) and aligned on the onset of blanking in **A–C**. Cells in **A** were tested when target blanking was applied more than 150 ms before the cells increased their activity ("before" group). Cells in **B** were tested when target blanking was applied almost simultaneously with the increased discharge ("during" group). Discharge rate difference exceeded the plotting scale in **A** and **B** (*asterisks*). *Thick* and *dashed lines* in **C** show mean (±SD) difference in discharge rates of all cells tested in two monkeys (C *red*, N *black*) separately. **D** Mean eye velocity difference of the two monkeys with and without blanking of the tracking target aligned on the onset of blanking. *Arrows* during blanking depict onset of eye velocity decrease in two monkeys as indicated

guished; two cells increased, while four others decreased. Two of these cells (one increased, the other decreased) were observed when blanking was applied before, and the four others during, the phase that cells increased activity (Fig. 5A, B respectively). Since all four cells that showed decreases were recorded from monkey C, in Fig. 5C the mean difference (±SD; *dashed lines*) in discharge rates of all cells tested for the two monkeys were plotted separately. Discharge rate changed minimally during target blanking in monkey N (*black traces*), whereas discharge rate clearly decreased in monkey C (*red traces*) although there was quite a bit of variability.

To compare activity with the simultaneously recorded eye velocity, we subtracted eye velocity without blanking from eye velocity with blanking for each cell, and averaged them separately for the two monkeys in Fig. 5D. Average eye velocities decreased at ca 0.3 s (monkey C, *red*) and 0.4 s (monkey N, *heavy black*) after blanking the target. The decrease in discharge rate corresponds to an eye velocity decrease in monkey C (*red traces* in Fig. 5C, D), but in monkey N, discharge was relatively constant in contrast to the consistent decrease in eye velocity during the later half of the blanking period (cf. *black traces* in Fig. 5C, D). These results suggest that although the activity of periarcuate pursuit neurons during blanking can be explained in part by eye velocity, that discharge may also reflect some other signals as well (see below and Discussion).

Of the 24 pursuit neurons examined, 17 were tested for visual responses while the monkeys fixated a stationary spot in the second task condition as described below. Of these 17, 8 showed visual response, while the remaining 9 did not. Five visually responding cells and 3 non-

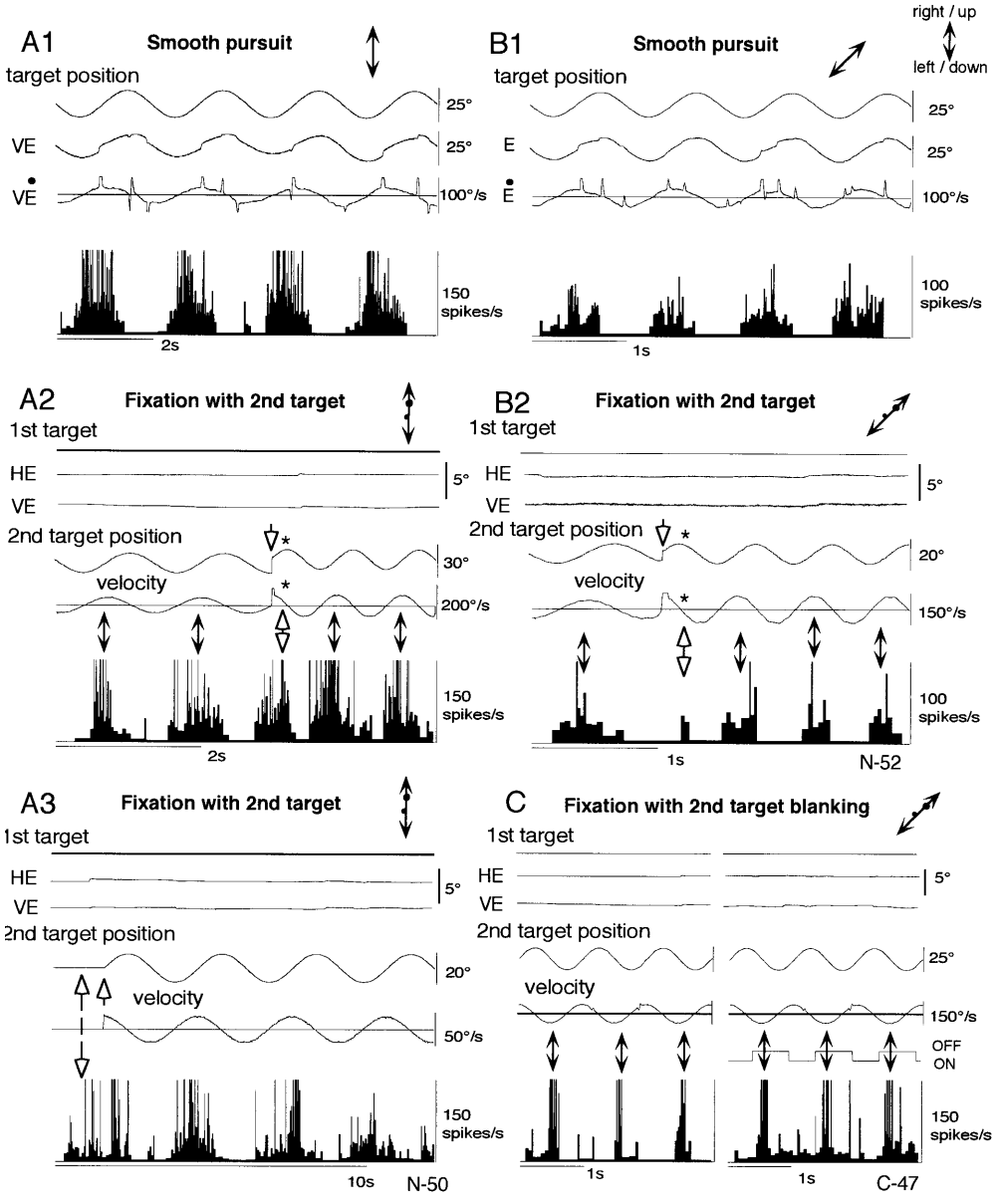

Fig. 6A–C Retinal image-motion-response of periarcuate pursuit cells. Responses of three different cells are shown together with eye position and velocity in **A**(*1–3*), **B**(*1, 2*), and **C**. **A***1* and **B***1* Responses during smooth pursuit. **A***2* and **B***2* Responses during abrupt changes of test target motion while the monkeys fixated a stationary spot (*downward open arrowheads*). *Double-headed open arrowheads* and *asterisks* Peak discharges of the two cells lagged due to the visual latencies. *Double-headed arrows* Peak discharge time of the two cells during consecutive cycles. **C** Comparison of responses when the test target was always on (*left*) and when it was extinguished as indicated (*OFF*, *right*). *Double-headed arrows* Peak discharge time during consecutive cycles. **A***3* Responses at the beginning of predictable target motion. E and Ė indicate radial eye position and velocity, respectively. Other abbreviations as in Fig. 2

visual cells were in the "before" group, while 3 visually responding cells and 6 non-visual cells were in the "during" group (Fig. 4A, B). Their responses during blanking of a tracking target were similar (Fig. 4A, B; see Discussion).

Visual response of periarcuate pursuit neurons: fixation with a second target

As reported previously, about half of periarcuate pursuit neurons also respond to visual target motion characterized by preferred directions similar to their smooth pursuit preferred directions (Fukushima et al. 2000a). In the present study, we tested a total of 80 cells in three monkeys (24 cells from monkey C, 54 cells from monkey T, and 2 cells from monkey N) by requiring the monkeys to fixate a stationary laser spot while a second laser spot moved sinusoidally (see Methods), and 54 of the 80 (68%) responded to the test spot motion.

As described in the Introduction, prediction must occur in the sensory and/or perception pathways as a visual response that anticipates the eventually relit visual target in order to overcome the long delays involved in processing visual motion information. Such predictive discharge is seen in the visual response of our cells. Representative discharge is shown in Fig. 6 for three neurons. Two cells shown in Fig. 6 (A*1*–A*3* and B*1*–B*2*) had upward (A*1*) or oblique (up and right, B*1*) preferred directions during smooth pursuit. When the monkey fixated a stationary spot (first target) while the second target moved sinusoidally (Fig. 6A*2*, B*2*), these cells also responded to the second target motion when it moved up (A*2*) or up and right (B*2*) with their peak discharge near peak target velocity. When the motion of the second target was changed abruptly to a higher frequency along

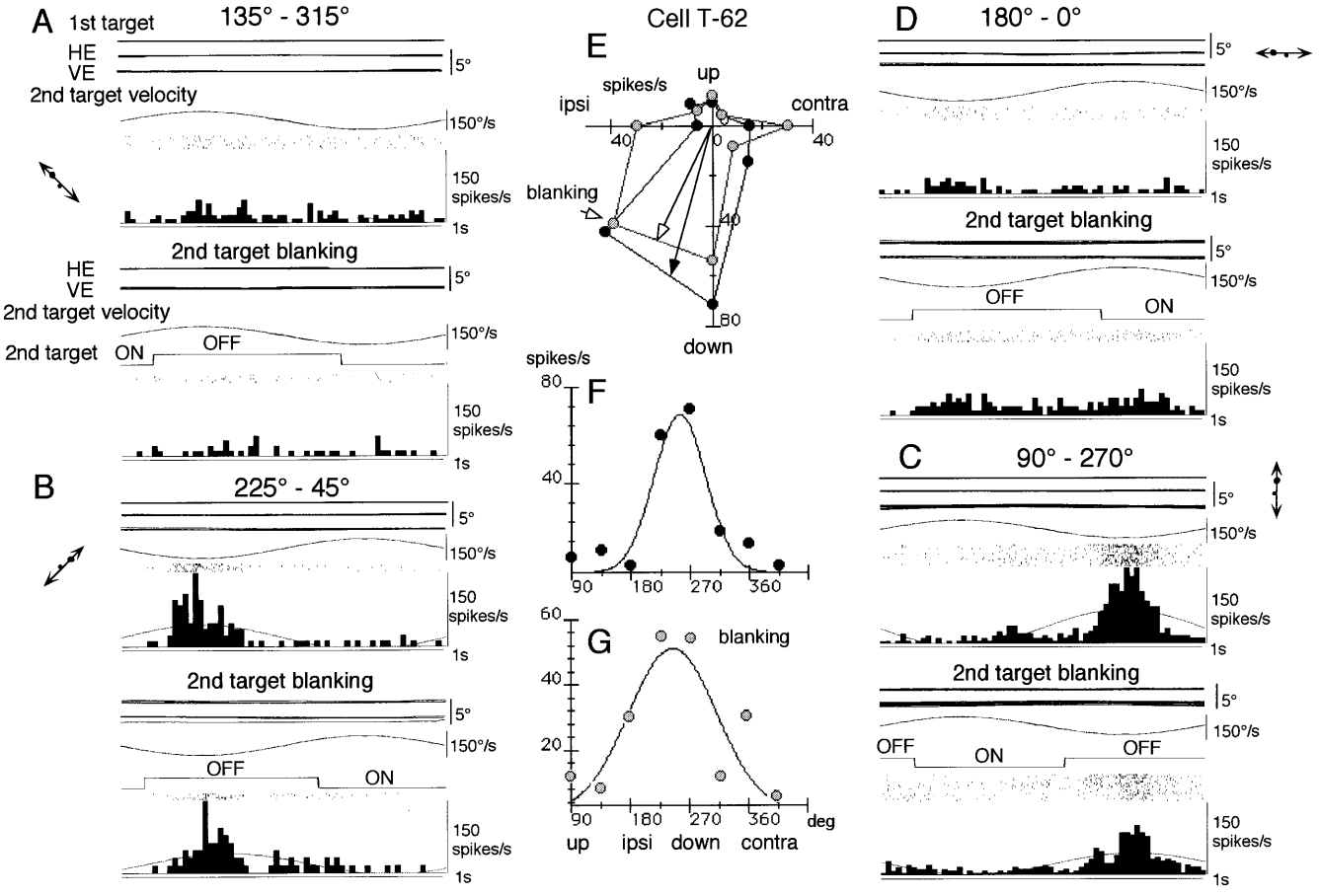

Fig. 7A–G Retinal image-motion-response of a periarcuate pursuit cell. In all traces, the monkey fixated a stationary spot while the second test spot moved sinusoidally along four different directions (**A–D**). *Upper panels* for **A–D** are horizontal and vertical eye position (*HE*, *VE*), second target velocity, and rasters and histograms of cell responses when the second target was always visible. In the *lower panels* for **A–D**, the second spot was extinguished for more than half of each cycle (0.6 s at 1 Hz) as indicated (*OFF*). Traces in **B–D** have similar arrangements as in **A**. **E–G** Directional tuning of this cell (**E**) with (*gray circles*) and without (*filled circles*) blanking the second target, and Gaussian fits with (**G**) and without (**F**) blanking

their preferred directions (Fig. 6A*2*, B*2 downward open arrowheads*), the visual response of these cells showed a clear phase lag due to the visual latencies, responding approximately in phase with peak target position (Fig. 6A*2*, B*2 asterisks*). However, these delays were compensated in the very next cycles, in which these neurons responded approximately in phase with peak target velocity (i.e., shifts ca 90°, Fig. 6A*2*, B*2 double-headed arrows*). These observations suggest that visual delays involved in processing target motion information are already compensated at the level of periarcuate pursuit neurons when target movement is sinusoidal.

Predictive visual responses of periarcuate pursuit neurons are also clearly seen during target blanking when target motion was sinusoidal. This is the task condition that we assumed would reveal visual prediction but without actual retinal image-slip input (see Methods) and is illustrated in Fig. 6C for another neuron with an oblique preferred direction. Blanking was timed to occur before the second target changed direction, and this cell discharged clearly during target blanking (Fig. 6C, compare *left* and *right*). Moreover, predictive responses are also seen in anticipation of second target movement following a short pause (Fig. 6A*3*) during testing in blocks, similar to the test during smooth tracking (Fig. 2B*2*). A representative discharge is shown in Fig. 6A*3*. This cell started discharging (open arrowheads connected by dotted line) before the target actually moved (upward open arrow). Similar observations were made in ten other cells that showed visual response in the fixation with second target task. These cells increased their discharge above the resting rate of each neuron preceding target movement by 0–1.1 s with the mean of 0.49 s, suggesting that such activity also reflects anticipation of target movement.

Effects of blanking the second target

To analyze predictive visual discharge, we quantified responses during blanking of the second test spot by averaging cell discharge using raster histograms. Representative discharge is shown in Figs. 7 and 8 for two neurons. In Fig. 7, the response to different stimulus directions is shown together with superimposed eye position traces (Fig. 7A–D *upper panels* in each section). This cell had a

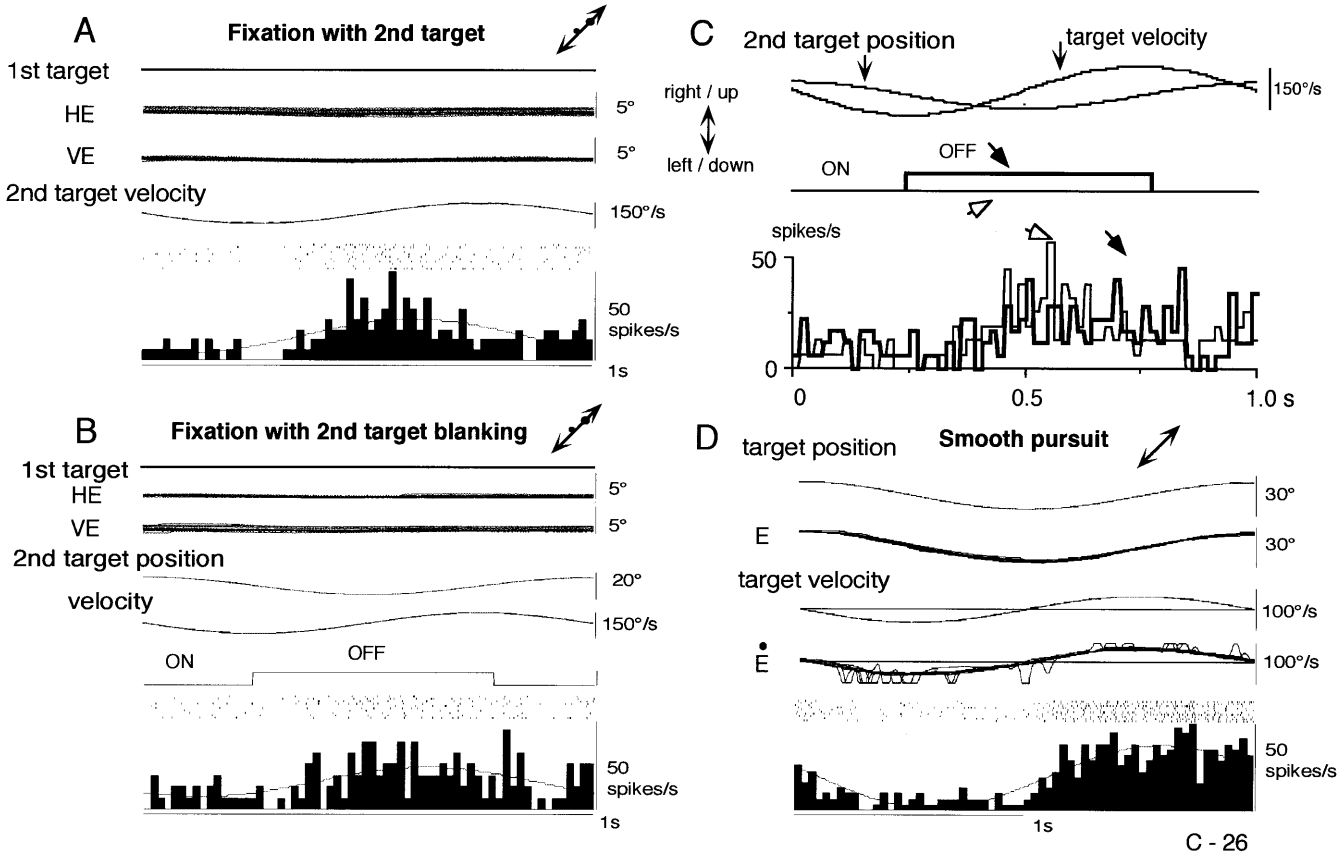

Fig. 8A–D Example of retinal image-motion-response of another cell. **A**, **B** Cell response with and without blanking the second target as indicated (*OFF*) during fixation of the first target. **C**, **D** Comparison of mean discharge rates during the two conditions and response of this cell during smooth pursuit, respectively. *Open arrows* Cell discharge (*thin line*) when target was on. *Filled arrows* Cell discharge (*thick line*) when target was blanked during the period indicated (*OFF*)

robust visual response when the second target was moved down and left (Fig. 7B, C). Its preferred direction, calculated by Gaussian fit, is shown in Fig. 7E (*filled circles* with *filled arrow*) and F. We extinguished the second target for almost half of each cycle while the monkeys continued fixating the first stationary spot which was on all the time. As before, in this task, blanking was applied prior to a sinusoidally moving target's change in direction. As illustrated in the *lower panels* of Fig. 7B, C, this cell discharged clearly when the second test spot was moved down and left even though its actual movement to those positions was not seen (*OFF*). The response magnitudes were slightly decreased compared to the responses in the presence of the actual spot (Fig. 7B, C, *lower* vs *upper panels*). Since discharge modulation of this cell was not observed in response to similar blanking when the second target was moved up and right (Fig. 7A, D *lower panel*), the discharge was not due to simple blanking of the moving spot. This result indicates that predictive visual responses were direction specific and that the preferred activation direction for the second target changed very little during blanking (Fig. 7E *gray circles* with *open arrow*, G).

The neuron shown in Fig. 8A, B had an oblique preferred direction during smooth pursuit (Fig. 8D). When the monkey fixated a stationary spot (Fig. 8A), this cell also had a visual response to the test spot with a similar preferred direction but with the phase almost 90° advanced compared to the response during smooth pursuit (Fig. 8D vs A). Since its activity was not modulated when the test spot remained stationary (not shown), the phase-advanced response (Fig. 8A) must have been induced by acceleration of test target motion. Discharge modulation along the preferred direction of the test spot was also apparent during blanking (Fig. 8B). Comparison of averaged cell activity indicates that the modulation amplitude was only slightly reduced during blanking (Fig. 8C). Since the monkeys fixated the first stationary spot well in all these conditions (Figs. 7A–D, 8A, B *HE* and *VE*) and since we accepted only those traces in which eye position changes were <1° during each cycle, eye velocity per se could not have contributed significantly to the response during these tasks (see Methods). Rather, these neurons responded to motion of the second target and activity of these cells could be induced without the presence of the actual retinal image-slip.

Activity of a total of 18 pursuit neurons (9 from monkey C, 9 from monkey T) was examined in this task (1 Hz, ±10°). The majority of them (n=12) showed peak discharge near (within 45°) peak target velocity, and peak discharge of the remaining 6 cells was near peak

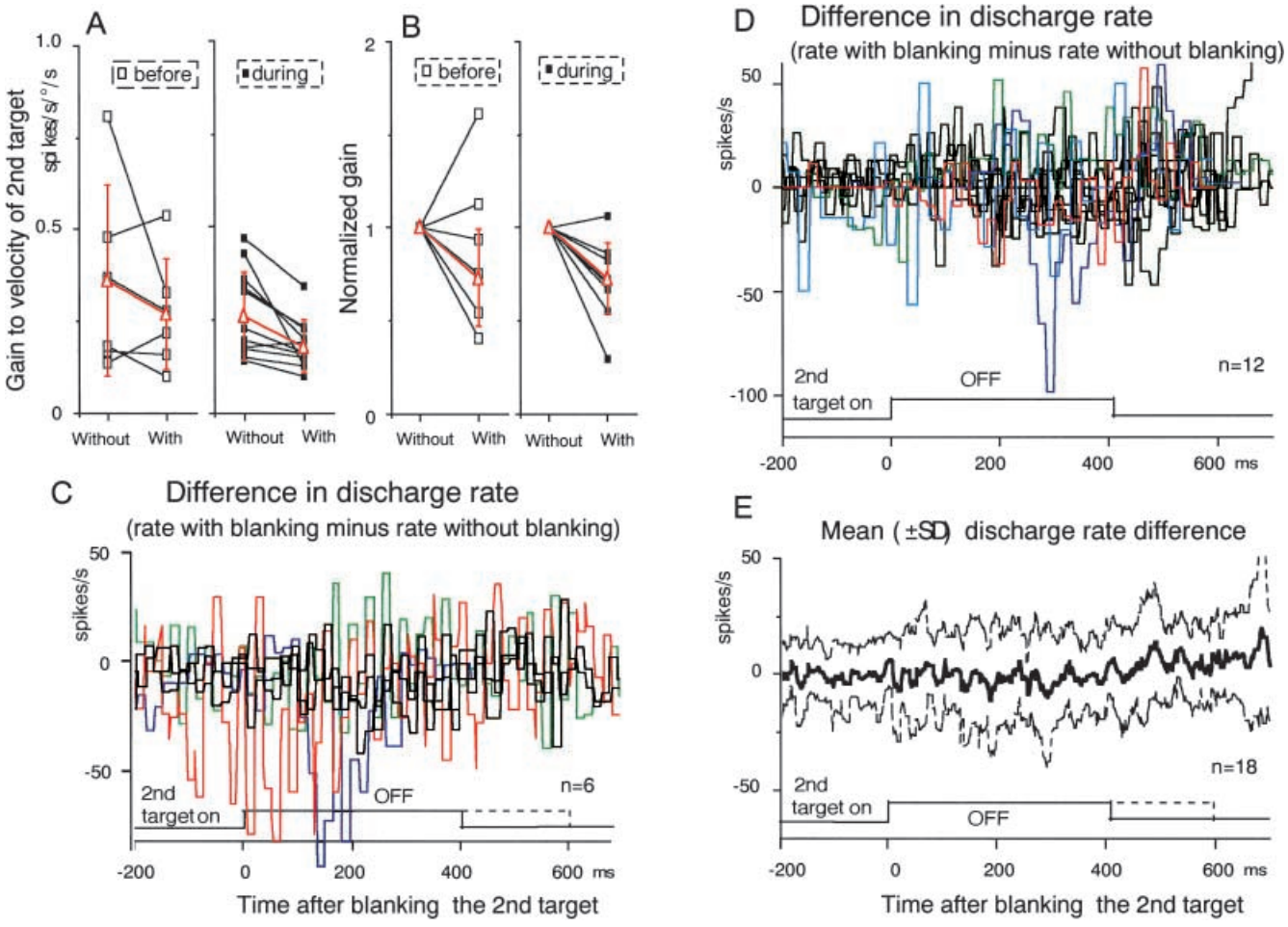

Fig. 9A–E Comparison of pursuit cell gains to velocity of test target motion with and without blanking of the test spot. **A**, **B** *Open squares* plot gains of cells when target blanking was applied more than 100 ms before these cells increased activity ("before" group). *Filled squares* plot gains of cells when target blanking was applied almost simultaneously with increased discharge ("during" group). Cells shown in **A** and **B** are different. Values of the same cells are connected by *lines*. *Red triangles* and *bars* show mean (±SD) values. **C**, **D** Differences in discharge rates with and without blanking the second target. Discharge rate without blanking was subtracted from discharge rate with blanking for each cell in the two groups (**C** before; **D** during) and are aligned on the onset of blanking. **E** *Thick* and *thin lines* show mean (±SD) discharge rate differences of the 18 cells. Target was extinguished during the periods indicated (*OFF*)

target acceleration. Of the total, 6 cells were tested by applying blanking at least 100 ms before the cells increased their activity in all trials (4 cells in monkey C, 2 cells from monkey T; Figs. 7, 8). In the remaining 12 cells, blanking was applied almost simultaneously with the onset of cell discharge (see, for example, Fig. 6C) and as a result the target was turned off during the early phase when these cells normally increased activity. The blanking period was 600 ms in 4 cells of the first condition, and in the remaining cells the blanking period was 400 ms. The results obtained in these two groups of cells ("before" and "during", respectively) were analyzed separately and are summarized in Fig. 9. Gain values calculated by fitting a sinusoid are plotted in Fig. 9A for each cell in the two groups. Their distributions are similar and show that mean (±SD) cell gains decreased during target blanking from 0.36 (±0.26) to 0.27 (±0.15) and from 0.26 (±0.12) to 0.18 (±0.07) spikes/s per °/s for the two groups, respectively (Fig. 9A), and the overall mean gains decreased from 0.29 to 0.21 spikes/s per °/s. Normalized gain values (re control gain without blanking) are plotted in Fig. 9B for the two groups. Mean (±SD) normalized gains decreased to 0.74 (±0.26) and 0.73 (±0.19) of the control gain for the two groups, respectively (Fig. 9B).

As we did for the analysis in the first task condition (Fig. 5A–C), we further quantified changes in discharge rate by subtracting discharge rate without blanking from that with blanking. Differences in discharge rates of cells in the two groups ("before" and "during") are plotted separately in Fig. 9C, D, aligned on the onset of blanking. Although there were differences in discharge rates of individual cells, the differences of the majority of cells remained near zero during blanking. Only 7 cells exceeded their maximal pre-blank difference; 3 cells increased, while 4 others decreased. Three (1 increased, 2 decreased) of the 7 cells were tested in the "before" condition, and 1 cell of the 3 decreased activity before the onset of blanking (Fig. 9C). The remaining 4 cells were tested in the "during" condition (Fig. 9D). Differ-

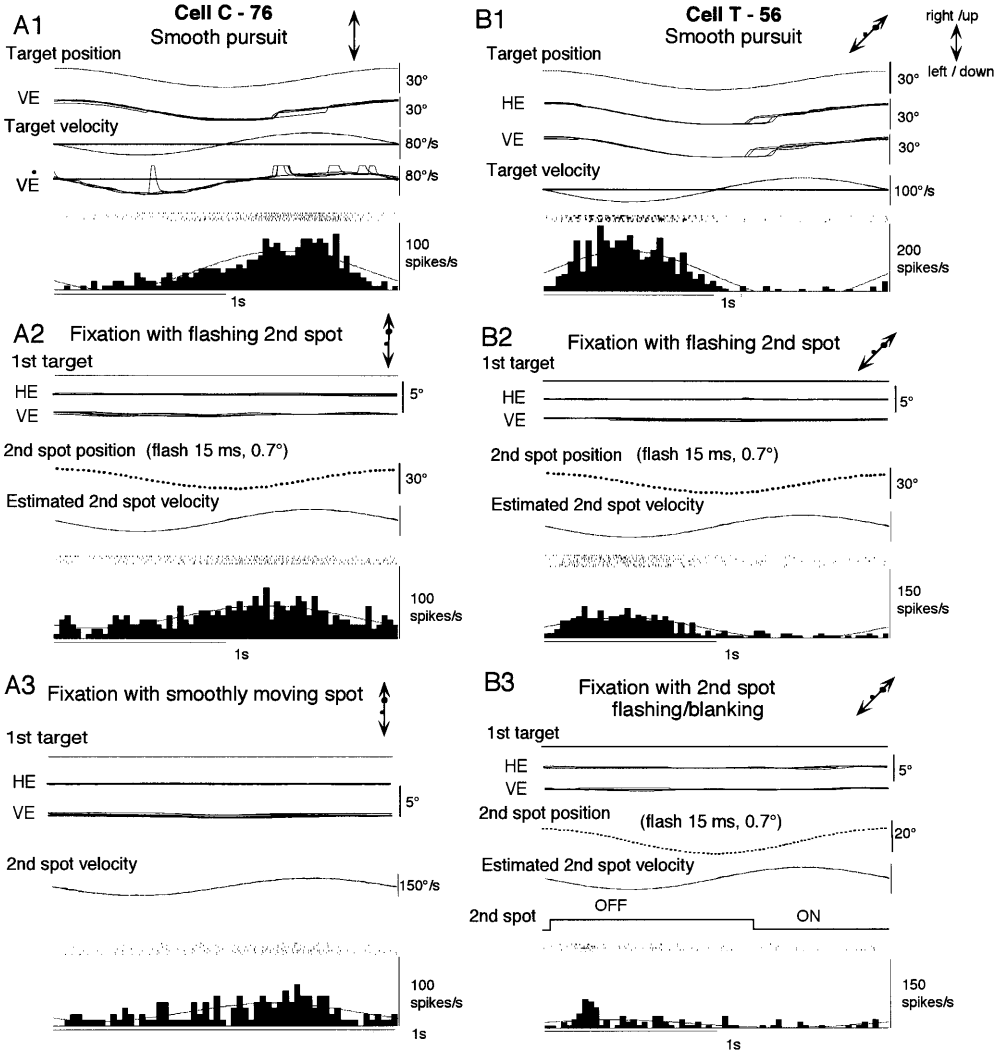

Fig. 10A, B Responses of periarcuate pursuit cells to a sequentially flashing second spot. **A**(*1–3*) and **B**(*1–3*) are two different cells. **A***1*, **B***1* Responses during smooth pursuit along each cell's preferred directions. **A***2*, **B***2* Responses to a sequentially flashing second spot while the monkeys fixated the first stationary spot (flash duration 15 ms, flash-to-flash distance 0.7°). **A***3* Response to a smoothly moving second spot while the monkey fixated the first stationary spot. **B***3* Response when the second flashing spot was extinguished for about half of each cycle as indicated (*OFF*)

ences in discharge rates of these 7 cells are plotted in colors (Fig. 9C, D). Since the results obtained in the two groups were similar except for 1 cell (*red trace* in Fig. 9C), in Fig. 9E the mean (±SD) difference in discharge rates of all cells tested for the two monkeys were plotted together. The average discharge rate difference decreased minimally during blanking with the overall mean discharge rate differences during the first 200 ms blanking period (0–200 ms) and the next 200 ms (200–400 ms) being –2.4 and –3.6 spikes/s, respectively (Fig. 9E). These values were less than one-third of the mean amplitude of modulation without blanking (11.8 spikes/s).

None of the 18 cells showed a significant response when blanking was applied in the direction orthogonal to the preferred direction (see, for example, Fig. 7A, D *lower panels*). This indicates that discharge modulation during blanking is specific to invisible target motion in the preferred directions. This was further confirmed in 5 of the 18 tested neurons in which we calculated preferred directions during blanking by Gaussian fits as shown in Fig. 7E, G, and all were within 90° of the control directions. These results, therefore, indicate that discharge modulation is qualitatively similar to that induced by retinal image-slip and can be induced without actual retinal image-motion for periarcuate pursuit neurons.

Visual response of periarcuate pursuit neurons: fixation with a second spot flashing

Since in the last task the smoothly moving second spot was visible to the monkeys for about half of each cycle (Figs. 7, 8), it is possible, if unlikely, that the putative visual response of periarcuate pursuit cells during blanking of the second spot was due to a delayed response to retinal image-slip information presented during the remaining half of each cycle. To examine this possibility and to minimize retinal image-slip, we flashed the second spot sequentially instead of moving it smoothly (see Methods). A total of 28 pursuit cells was examined in this task condition (9 cells from monkey C, 19 cells from monkey T). The majority (26 of the 28) responded using the continuously illuminated smoothly moving second spot (see, for example, Fig. 7). When the second spot was flashed, most of them (25 of the 28) also responded.

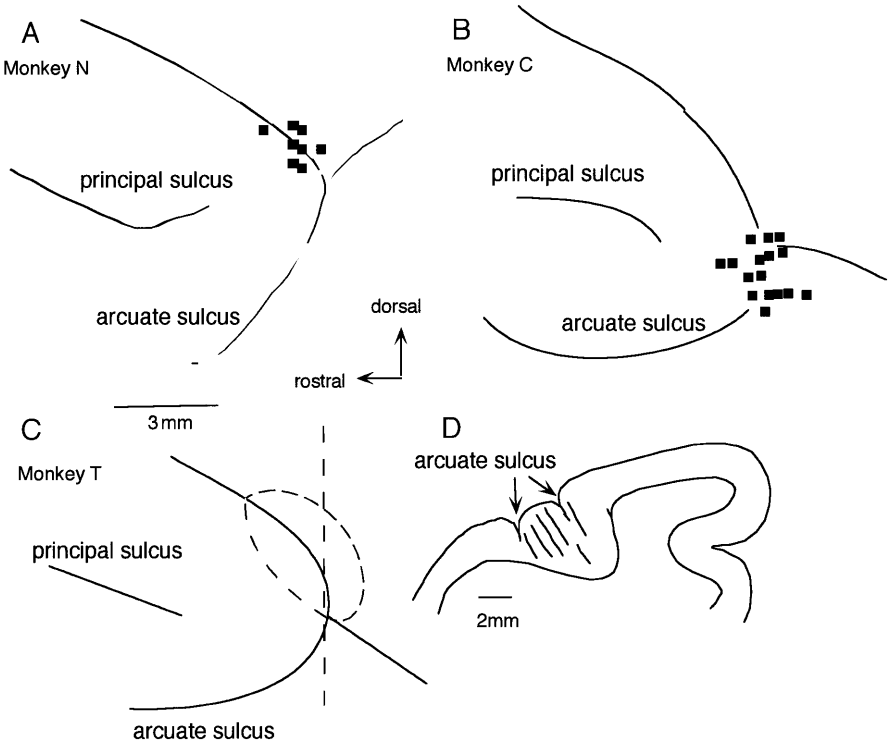

Fig. 11A–D Recording locations. **A**, **B** Summary of top view of the left periarcuate cortex of two monkeys and penetration sites where pursuit cells were recorded. **C**, **D** Recording locations of the third monkey. *Dashed area* in top view (**C**) of arcuate sulcus region indicates entry points of tracks, and cross-section (**D**) through area indicated by *dashed line* shows trajectory of tracks containing responsive neurons

Representative responses are shown in Fig. 10 for 2 cells. These cells had vertical and oblique preferred directions during pursuit (Fig. 10A*1*, B*1*, respectively). When the flashing second spot was presented, most of these cells also responded clearly to such stimuli with preferred directions similar to those during pursuit (Fig. 10A*2*, B*2*). It should be pointed out that the monkeys fixated the stationary fixation spot well in all these conditions (*HE* and *VE* in Fig. 10A*2*, B*2*). Thus, discharge modulation during these task conditions does not reflect eye velocity. Rather, these neurons responded to motion of the flashing spot.

To compare response magnitude of the sequentially flashing spot versus the continuously moving spot, we calculated amplitude of modulation from the sine-fit. The mean (±SD) amplitude of modulation to the flashing second spot (at 0.5 Hz, ±10°) was 11.7 (±7.4) spikes/s, while that of the same cells to a smoothly moving target (at 1.0 Hz, ±10) was 11.8 (±9.4) spikes/s. Thus, the response magnitudes were identical during these two kinds of stimulus presentation (Fig. 10A*2* vs A*3*). For comparison, we also calculated mean gain (re stimulus velocity) of these cells during smooth pursuit (at 0.5 Hz, ±10°) and fixation with a smoothly moving second target (at 1 Hz, ±10°). Mean (±SD) gains of the 14 cells in these two task conditions were 0.56 (±0.37) and 0.21 (±0.17) spikes/s per °/s, respectively. These gain values are similar to our previous results using a different method for calculation of velocity sensitivity (0.58 vs 0.21 spikes/s per °/s; Fukushima et al. 2000a). These results indicate that discharge modulation as large as that for retinal image-slip (but smaller than that for smooth pursuit) can be induced by a sequentially flashing spot without actual retinal slip (Fig. 10A*2* vs A*3*). Furthermore, even without the presence of actual spot, all cells tested (n=6) responded weakly but clearly during blanking of the sequentially flashing second spot while the monkey continued fixating the first stationary spot (Fig. 10B*2* vs B*3*).

Recording locations

Recording locations of three monkeys are summarized in Fig. 11A–D. Entry points of tracks in monkeys N and T (Fig. 11A, C, D) were slightly dorsal compared to those in monkey C (Fig. 11B). Lesions and recording tracks were found in the fundus and posterior bank of the arcuate sulcus (Fig. 11D) and the superior arcuate sulcus near its medial tip, similar to the areas reported for smooth pursuit areas in previous studies (MacAvoy et al. 1991; Gottlieb et al. 1993, 1994; Tian and Lynch 1996a, b; Tanaka and Fukushima 1998; Fukushima et al. 2000a). These recording locations correspond to the pursuit areas of the FEF reported in those previous studies. We did not find any clear localization for cells that showed predictive visual response compared with others that did not. We often observed both types of cells in the same recording tracks. The fourth monkey (H) is still being used for other experiments.

Discussion

Prediction-related activity of periarcuate pursuit neurons during tracking

Our results demonstrate that the response delays involved in processing visual motion information during abrupt motion of a tracking target (Fig. 1B) are already compensated at the level of periarcuate pursuit neurons once a predictable sinusoidal target trajectory has been established. During sinusoidal tracking, at least eight out of ten cells in which target blanking was applied more than 150 ms before these cells increased activity, discharged appropriately during the initial 500 ms of blanking (Fig. 5A). Since visual latencies of periarcuate pursuit cells were ca 100 ms in previous studies (Fukushima et al. 2000a), it is unlikely that their responses during blanking were induced by target motion before blanking. Moreover, since during blanking many pursuit cells discharged following initially zero rates (Fig. 3), their activity during blanking cannot be explained by simple maintenance of tonic discharge before blanking. These observations, therefore, indicate that periarcuate pursuit neurons may be involved in predictive smooth pursuit eye movements by compensating for response delays and discharging appropriately for invisible target motion during blanking.

Although our cells showed significant modulation with blanking (Fig. 4A, B), response gains of the majority of cells decreased in association with eye gain decrease (Fig. 4C, D), suggesting that their activity might reflect eye velocity commands produced during predictive tracking eye movements (see, for example, Fig. 3A). It has been shown that discharge of periarcuate pursuit neurons is closely associated with eye velocity during tracking of a sinusoidally moving target at 0.5–1 Hz (Gottlieb et al. 1994; Fukushima et al. 2000a). For six cells we tested whether discharge modulation is explained by eye velocity during the sinusoidal tracking with blanking condition. We first fit discharge modulation by eye velocity alone and then by adding an eye acceleration component or target velocity and acceleration components. We compared fitting among these conditions assuming linear addition of these variables. Adding eye acceleration to eye velocity, fitting was only slightly improved. Adding the target motion components also improved the fit but only slightly. Therefore, our fitting suggests that discharge modulation of these pursuit cells during sinusoidal smooth tracking is most parsimoniously explained by eye velocity alone.

However, the discharge of some periarcuate pursuit neurons during blanking may also reflect some other signals as well for the following reasons:

1. There was a clear dissociation between final motor output and discharge of some cells, since those cells discharged before the onset of predictable pursuit (Fig. 2B*2*) and some increased activity during target blanking despite consistent decreases in eye velocity (Fig. 3B).
2. At least in monkey N, discharge of similar magnitude was observed with and without target blanking despite a decrease in eye velocity (Fig. 5C, D).
3. About half of the pursuit cells tested for target blanking (see, for example, Fig. 3) showed a visual response, and during the second spot task condition with blanking, these cells carried predictive "visual" responses that did not require actual presence of target motion. As discussed below, discharge modulation during this task condition is best explained by target motion, because eye velocity was virtually zero.

Visual response of periarcuate pursuit neurons and predictive "visual" response

About half of periarcuate pursuit cells carry visual target motion information (Fukushima et al. 2000a). This study shows that visual response delays seen during abrupt onset of target motion are already compensated at the level of periarcuate pursuit cells once a predictable target motion trajectory is established (Fig. 6). This finding suggests that response delay compensation during tracking (Fig. 1) indeed occurs for visual components. This is consistent with our results showing that delay compensation was observed for visually responding pursuit cells (Fig. 1B *filled squares*). Although we observed response delay compensation in non-visual pursuit cells as well (Fig. 1B *open squares*), we do not exclude the possibility that it came from visually responding periarcuate pursuit cells.

Our results also show that discharge of all visually responding cells tested was modulated significantly during blanking of the second test spot (Figs. 7, 8, 9). Since the overall mean gains decreased from 0.29 spikes/s per °/s without blanking to 0.21 spikes/s per °/s with blanking (Fig. 9A) and since the average discharge rate difference decreased by ca one-third of the modulation with actual target motion (3.6/11.8 spikes/s; Fig. 9E), retinal input indeed contributed to the visual response of these cells during blanking. Nevertheless, qualitatively similar discharge modulation, in terms of preferred directions and response magnitudes, were still induced even when the test target was blanked for about half of a cycle (Figs. 7, 8, 9). Moreover, it is unlikely that their responses during blanking were induced by target motion before blanking since at least 6 out of 18 cells discharged appropriately during blanking (Figs. 7, 8) when blanking was applied more than 100 ms before those cells normally increased activity. Furthermore, target motion information carried by periarcuate pursuit neurons does not require retinal image-slip that was presented for about half of each cycle when the smoothly moving spot was used (Figs. 6, 7, 8; cf. Mikami 1992; Thier and Erickson 1992). This is evidenced by the fact that the great majority of pursuit neurons responding to a smoothly moving spot (25 out of 28) responded similarly when this spot was flashed (see, for example, Fig. 10A*2*). These results indicate that prediction-related "visual" activity of many periarcuate

pursuit neurons contains extracted visual components that reflect direction and speed of the reconstructed target image and that these neurons could discharge appropriately up to 400 ms after blanking in anticipation of incoming target motion (Fig. 9). Since motion prediction requires motion memory, we do not exclude the possibility that discharge modulation reflects memory for target motion (Droll et al. 2000). Previous studies in our laboratory reported some periarcuate pursuit cells showing a buildup activity unrelated to pursuit direction and other non-pursuit cells showing only a buildup activity unrelated to target motion-direction (Figs. 14 and 15 of Tanaka and Fukushima 1998). Their activity may have been related to anticipation of target motion and/or timing of motion onset. In this study, predictive discharge of our pursuit cells was direction-specific although their activity compensated for response delays (i.e., timing). This difference may be related to the different task conditions used in these two studies. We speculate that prediction contains both direction and timing components and that these two components may be processed separately in some task conditions.

Visual response characteristics of our cells seem to be similar to those reported for MST visual tacking neurons (Komatsu and Wurtz 1988a, b, c; Thier and Erickson 1992; Dicke and Thier 1999). Newsome et al. (1988) reported that the visual response of MST cells during smooth pursuit occurs even when the visual stimulus is applied outside the receptive field and before the eye movement (their Fig. 12). Since this does not happen during fixation, they interpreted their observations as expansion of visual receptive fields associated with smooth pursuit. Although the exact neural mechanism for this expansion is unknown, it may include predictive components that are also present in the MST area.

It is well known that MST cells respond to flashed targets (cf. Thier and Erickson 1992; Dicke and Thier 1999; also Mikami et al. 1986; Mikami 1992) so it is plausible that visual responses of periarcuate pursuit cells arise in the MST area, including responses to a sequentially flashing second spot in this study. Reciprocal connections between the periarcuate pursuit-related areas and MST area (Tusa and Ungerleider 1988; Stanton et al. 1993, 1995; Tian and Lynch 1996a, b) may contribute to the similarity in the discharge characteristics of these two areas.

Since not all pursuit cells responded to target motion (53% in Fukushima et al. 2000a, 68% in this study), it seems that periarcuate pursuit cells consist of functionally different cell groups (for example, visual-motor and motor cells), similar to prearcuate saccade cells (cf. Bruce and Goldberg 1985). Predictive visual response was also reported earlier in visual and visuomovement neurons in the FEF for the saccadic system (Umeno and Goldberg 1997), so it is not surprising that the FEF also participates in similar functions for the smooth pursuit system. A similar interpretation was advanced for predictive responses of FEF neurons to invisible target motion in the comparison of the saccade and pursuit responses (Ferrera and Barborica 2000; also Krauzlis and Stone 1999).

Possible role of periarcuate pursuit neurons in predictive visual response and smooth pursuit

Smooth pursuit can be performed efficiently up to 1 Hz even though the tracking target is invisible for a short period (see, for example, Becker and Fuchs 1985; Barnes 1993). Response delay compensation is necessary for this efficient performance (see, for example, Suh et al. 2000). Our results indicate that such delay compensation is already accomplished at the level of periarcuate pursuit neurons (Figs. 1, 6). Moreover, as discussed above, periarcuate activity during predictive tracking of an invisible target contained predictive "visual" components that reflect direction and speed of the reconstructed target image (see, for example, Fig. 7). These signals seem to be sufficient for estimates of target motion particularly its velocity (Robinson 1982). Although the responsible neural mechanisms for these signals are still unknown, our results indicate that periarcuate pursuit areas are involved in direction-specific predictive smooth pursuit and that the same circuitry, at least in part, is also used for processing of predictive visual signals about target velocity.

Normalized gain decrease of our cells during blanking seems similar when the monkeys tracked the target (0.83–0.64, Fig. 4E, F) and when they fixated a stationary target (0.74, Fig. 9B). Indeed, in one monkey (N) smooth pursuit eye movements were generated appropriately up to 0.4 s during blanking and pursuit cells discharged appropriately (Fig. 5C, D). However, in the other monkey (C) discharge during blanking was more variable and accompanied by poor smooth pursuit eye movements (Figs. 3B*3*, 4D, 5C). Despite poor tracking, pursuit cells in monkey C were also modulated appropriately in response to invisible target motion during blanking (Figs. 8, 9). We do not have a compelling rationale for these differences. However, this dissociation between predictive visual response and predictive smooth pursuit eye movements suggests that conversion of target motion signals into eye movement commands requires further processing which may have differed in the two monkeys for unknown reasons.

MacAvoy et al. (1991) reported that sequential surgical ablation of the bilateral periarcuate pursuit regions in the FEF, particularly the arcuate fundus, produce substantial deficits in the anticipatory initiation and predictive continuation of smooth pursuit (also Keating 1991). These observations may be explained by loss of prediction-related activity of periarcuate pursuit neurons observed in this study. Indeed, when the effects of muscimol injection into the periarcuate pursuit areas were tested in the same monkeys (monkeys N and C) in the same conditions as in the present study (Fig. 3) so that the monkeys had to perform smooth pursuit by changing direction without the presence of an actual target, they

were virtually unable to generate smooth pursuit in many trials. Instead, they tracked the invisible target with saccades (Fig. 5 of Fukushima et al. 1999a). These results suggest that the normal activity of the periarcuate pursuit areas is necessary for appropriate smooth ocular tracking in tasks that require prediction. However, more careful testing with smaller unilateral ablations including the arcuate fundus revealed that those lesions impair pursuit eye movements per se but preserve the predictions driving them (Keating 1993). These results suggest that although the periarcuate pursuit regions participate in predictive smooth pursuit, they are not the sole areas for this function. Neural correlates of inferred motion were also shown earlier in the posterior parietal cortex (area 7a; Assad and Maunsell 1995). Moreover, gaze-movement- and/or retinal image-slip-velocity-related signals are also found in the central thalamus (Schlag and Schlag-Rey 1986) in addition to the periarcuate cortical areas and MST area. It is possible that predictive functions in smooth gaze tracking including target velocity estimation are distributed in multiple circuits including these structures so that the effects of removal of only one structure may be less devastating.

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