J Physiol (2003), **551.2**, *pp.* 551–561
DOI: 10.1113/jphysiol.2003.042994

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Journal of Physiology

Selectivity of macaque ventral intraparietal area (area VIP) for smooth pursuit eye movements

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In the posterior parietal cortex (PPC) of the macaque, spatial and motion signals arising from different sensory signals converge. One of the functional subregions within the PPC, the ventral intraparietal area (VIP), is thought to play an important role for the multisensory encoding of self- and object motion. In the present study we analysed the activity of area VIP neurons related to smooth pursuit eye movements (SPEMs). Fifty-three per cent of the neurons (123/234) were selective for the direction of the SPEMs. As evident from control experiments, activity observed during smooth eye movements was more closely related to extraretinal signals than visual parameters. In addition, we examined the sensitivity of area VIP neurons for the velocity of SPEMs. Seventy-four per cent of the pursuit-related neurons had a significant velocity tuning. There was a clear preference for high velocities. Eighty-six per cent of the neurons preferred the highest pursuit velocity (40 deg s^{-1}) employed in our study. In everyday life, high pursuit velocities most frequently occur if the pursuit target is located in near-extrapersonal space, i.e. the action space of the head. Together with previous findings, the current results thus suggest that the information provided by VIP neurons may be used to encode motion in near-extrapersonal space and to guide and co-ordinate smooth eye and head movements within this very part of space.

(Received 14 March 2003; accepted after revision 23 June 2003; first published online 25 June 2003)
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In primates the visual system is the most highly developed sense. The receptor stage, i.e. the retina, contains a specialised area with highest spatial resolution: the fovea. If we want to gain detailed information about a particular object, the gaze is adjusted such that the image of this object falls onto the fovea. If the object of interest moves, its image has to be stabilised on the fovea by matching eye velocity to target velocity and correcting for positional errors. The respective eye movements are called smooth pursuit eye movements (SPEMs). Such eye movements are mainly controlled on the basis of afferent information about visual motion on the retina ('retinal slip') in combination with extraretinal information about eye movements and eye position (for review see Ilg, 1997). Different cortical and subcortical brain regions have been extensively studied regarding their role in the generation of SPEMs. One principle question in those studies was whether the pursuit activity of the neurons in these areas is more closely related to visual factors, i.e. retinal slip information, or whether it reflects extraretinal information. However, high gain SPEMs are only possible when a moving visual target is present. Differentiation between visual and extraretinal information is therefore not directly possible. To distinguish between these two cues several experimental controls have been introduced. When the target of the SPEM is extinguished for a brief time interval ('a blink') in the order of 100–200 ms during steady state pursuit, the eye movement can be maintained (Becker & Fuchs, 1985; Morris & Lisberger, 1987; Ilg & Thier, 1997). By using this or other experimental paradigms such as stabilisation of the image on the retina, the functional characteristics of the pursuit activity within the different brain areas have been established. The most extensively studied cortical areas of the pursuit system are the medial temporal area (MT) and the medial superior temporal area (MST). Area MT has been shown to be crucial for the analysis of retinal slip information, whereas area MST combines visual with extraretinal information (Newsome *et al.* 1988; Thier & Erickson, 1992). Other cortical areas with pursuit-related activity are the frontal eye fields (FEF), supplementary eye fields (SEF), the lateral intraparietal area (LIP), area 7a and area VIP (Lynch, 1987; Colby *et al.* 1993; Gottlieb *et al.* 1993; Bremmer *et al.* 1997*a*; Shi *et al.* 1998; Missal & Heinen, 2001; Tanaka & Lisberger, 2001). While the characteristics of the pursuit activity in areas MT and MST and the frontal regions have been extensively studied, the functional role of other areas is poorly understood (for review see Ilg, 1997; Goldberg, 2000).

In our present study we therefore aimed at characterising the pursuit-related activity of one of the parietal areas (area VIP) in more detail. Up to now, the existence of pursuit-related activity in this area has only been

demonstrated qualitatively for a very small sample of neurons (Colby *et al.* 1993). The present study thus addressed several questions. First, we wanted to determine the proportion of neurons sensitive to SPEMs in a large set of neurons. In addition, we analysed the distribution of preferred pursuit directions and velocities to test how neuronal activity is linked to particular pursuit parameters. Finally, we addressed the question whether pursuit-related activity in area VIP is caused by visual motion on the retina or whether it reflects extraretinal information about the executed eye movement.

METHODS

We recorded neuronal activity in area VIP in two male awake behaving monkeys (*M. mulatta*: 9.2 kg and 9.5 kg). All treatment of the animals such as housing and surgical procedures was in accordance with German and internationally published guidelines on the use of animals in research (European Communities Council Directive 86/609/ECC).

Animal preparation and experimental equipment

A first surgery served to prepare the animal for the experiments. The initial anaesthesia consisted of an injection of 0.1 ml (kg body weight)$^{-1}$ ketamine hydrochloride (Ketanest, Pare-Davis, Munich). Subsequently, anaesthesia was maintained at a stable level by I.V. injection of 0.5–1 ml pentobarbital as required (Narkoren, 1:4 diluted). During this surgery the animals received a head holding device. In order to monitor eye movements, two scleral search coils were implanted (Judge *et al.* 1980). On the basis of previously measured MRI scans, we placed the recording chamber for microelectrode penetrations across the intraparietal sulcus at an angle of 45 deg relative to the vertical at P 4 L 13.5 in the first animal (H) and at P 3 L 15 in the second animal (C). In one animal we recorded from the left cortical hemisphere and in the other animal from the right. The recording chamber and head holder were fixed to the skull via self-tapering screws. The whole implant was covered and stabilised with dental acrylic, self-tapering screws (Technovit 4004). We monitored any discomfort following the surgery based on physical (e.g. swelling, redness etc.) and behavioural (e.g. diminished appetite, vocalization, reluctance to move) criteria. We treated the animals with a non-steroidal anti-inflammatory analgesic (Tylenol) in tablet form as long as the discomfort persisted (dosage: one tablet corresponding to 8 mg kg^{-1} of the active agent (Acetaminoprophen) up to six times a day depending on the intensity of the pain). The animals were allowed to recover fully from surgery before we performed the electrophysiological recordings.

During experiments, the monkeys were seated in a primate chair with the head fixed. For each correct trial the monkeys received a liquid reward. We used PC-based in-house software (NABEDA developed by Dr M. Pekel) to control the stimulation and data acquisition. For each penetration we determined the location of area VIP by the position of the electrode in the chamber relative to the MRI scans and by physiological criteria (e.g. direction-selective responses to visual stimuli). Usually, a recording session lasted up to 3 h. After we had finished all experiments the animals were killed with an overdose of pentobarbital (Narkoren, at least 1 ml (kg body weight)$^{-1}$). Histological analysis verified that recordings had been performed in area VIP.

Paradigms

All visual targets and stimuli used in the experiments were back-projected onto a translucent screen, which was located at a distance of 48 cm in front of the monkey. The screen covered the central 90 deg × 90 deg of the visual field. We used two different projection systems:

1. A mirror galvanometer to project targets for the smooth pursuit paradigms. A computer controlled and amplified voltage in the range of ± 5 V controlled the position of the low-pass damped mirror and thereby the position of the target on the screen.

2. A Silicon Graphics Workstation (Indigo High Impact) to generate complex visual stimuli. The visual stimuli were generated online on the workstation and back projected via a video projector (ELECTROHOME, ECP 4100) onto the projection screen.

Pursuit paradigms. All pursuit experiments were performed in darkness, i.e. luminance was below 0.01 cd m^{-2}. Lights were switched on for a few minutes prior to a new set of trials, resulting in an average luminance within the visual field of the animal of 8 cd m^{-2}. Since each set of trials lasted less than 5 min, this procedure prevented the monkeys from getting dark adapted during the experiments. A red light emitting diode (LED) (diameter 0.8 deg, luminance 0.4 cd m^{-2}) served as pursuit target and was moved across the projection screen by means of the mirror galvanometer described above.

Two different pursuit paradigms were used. The first was used to determine the influence of the pursuit direction on the cell activity and was termed the 'direction paradigm'. It consisted of a modified version of Rashbass's step ramp task (see Fig. 1; Rashbass, 1961). The pursuit directions of the different trials varied in pseudo-random order between upward, leftward, downward and rightward. After an initial fixation period of 800 ms the target was displaced 10 deg in the direction opposite to the upcoming pursuit direction and immediately began to move at 10 deg s^{-1} for 2100 ms. After 1600 ms the target was switched off for 200 ms ('blink period'). Since the blink period always occurred at the same point in time, the animals might have anticipated the blink, resulting in steady pursuit. Accordingly, the decrease in eye velocity expected during the blink period would be less pronounced than in pseudo-random trials with and without blink. In other words, anticipation might lead to an underestimation of the effect of the blink period on eye velocity.

The second paradigm was designed to test for the influence of pursuit velocity onto the cell activity and was termed the 'velocity paradigm'. During the velocity paradigm, the pursuit target moved with one of four different velocities (5, 10, 20 and 40 deg s^{-1}) in the preferred pursuit direction of the neuron (previously determined with the direction paradigm). The size of the initial step of the pursuit target and the pursuit duration for each velocity was again adjusted so that the target trajectory was always centred on the screen. For the slowest movement (5 deg s^{-1}), the size of the initial step was 5 deg, for the pursuit velocity of 10 deg s^{-1} it was 10 deg and for the remaining two velocities (20 and 40 deg s^{-1}) it was 20 deg. The duration of the pursuit phases for the first three velocities (5, 10 and 20 deg s^{-1}) was 2000 ms and for the highest velocity (40 deg s^{-1}) it was 1000 ms. The activity of a large number of neurons in area VIP is modulated by eye position (Bremmer *et al.* 1999). The design of the velocity paradigm prevented the possibility of eye position effects from affecting our results, since pursuit trajectories were centred on the straight-ahead position and eye position effects are

known to be linear across eye positions. In our velocity pursuit paradigm, the higher pursuit velocities result in more peripheral starting positions (to one side of straight ahead) and end positions (to the other side of straight ahead). Accordingly, lower levels on one side of straight ahead would be balanced out by higher levels on the other side (and vice versa). In other words, eye position effects cannot account for any observed velocity tuning.

Visual stimulation. The circular pathway stimulus consisted of a random dot pattern (500 white dots (diameter 1 deg, luminance 0.7 cd m^{-2}) on a black background), moving on a circular pathway in the frontoparallel plane. This means that the trajectory of the movement consisted of a continuously changing translation of the whole stimulus pattern (see Schoppmann & Hoffmann, 1976). The stimulation area covered the central 90 deg × 90 deg of the visual field. Six hundred milliseconds after the monkey had achieved central fixation, the stationary random dot pattern appeared on the screen. It remained stationary for 250 ms and then started to move for 2500 ms, i.e. 1.25 cycles with a velocity of 40 deg s^{-1}. It then remained stationary again for 250 ms and finally vanished from the screen. This visual pattern is arguably different from the visual stimulation with small stimuli, e.g. a pursuit target. Therefore, we compared the preferred direction of visual motion obtained by means of a small stimulus with the directional tuning obtained with the circular pathway stimulus for 21 neurons. Preferred directions were estimated qualitatively without further statistical testing. Nevertheless, these tests led to reliable estimates of the preferred direction for individual neurons (A. Kaminiarz, unpublished observations). As the direction selectivity did not differ for the two different stimuli in these control sessions, we only report the results of the more standardised circular pathway procedure.

Data analysis

Determination of directional and velocity tuning of the pursuit-related activity. To determine whether the neuronal discharge was significantly modulated by the pursuit, the activity of the neurons during the pursuit phase was determined for each trial. Since each target movement was preceded by a target step in the opposite direction to the upcoming pursuit, each pursuit phase began with a catch-up saccade. We determined the latency of the postsaccadic pursuit eye movement according to the following velocity criterion. The latency of the pursuit-related discharge was determined as the postsaccadic time at which the firing rate significantly ($P < 0.05$) exceeded baseline activity. The temporal window used for the analysis of pursuit directional tuning therefore started 350 ms after saccade offset (to avoid saccade-related effects) and ended at the end of the trial. We tested for differences between the four conditions (either different velocities or different directions of the pursuit) with a Kruskal-Wallis analysis of variance. If the null hypothesis, i.e. there are no differences in discharge for the different pursuit directions/velocities, was rejected ($P < 0.05$), the cell's activity was considered to be modulated by the pursuit parameter (either direction or velocity). In these cases a method of multiple comparisons (Siegel & Castellan, 1988) was used to determine which directions/velocities led to significant differences in neuronal discharge. For significantly tuned neurons we determined the preferred direction as the resultant vector of the mean activity during pursuit in the different directions. We defined the pursuit velocity leading to the strongest discharge as the preferred velocity. For both kinds of tuning the number of neurons preferring a particular direction/velocity was determined. With a χ^2 test we tested whether these counts were different from an expected uniform distribution.

We computed a direction index (DI) for all direction-selective neurons to obtain a measure for the strength of the direction selectivity:

$$DI = 1 - mDND/mDPD.$$

In this equation, 'mDND' is the 'mean discharge in null direction' and 'mDPD' is the 'mean discharge in preferred direction'. According to this definition, for example, a DI of 0.5 would be achieved if the activity in the null direction was half that of the activity in the preferred direction. A DI of 1.0 would indicate that the neurons did not discharge during SPEMs in null direction.

Determination of directional tuning for the visual stimuli. In order to determine whether the neurons were selective for the direction of the visual stimulation (i.e. the circular pathway stimulus) or not, the movement trajectory of the stimulus was

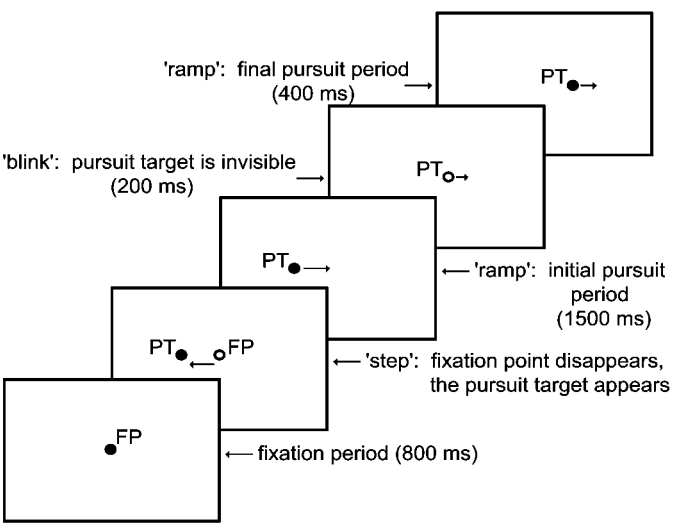

Figure 1. Example for one trial of the direction pursuit paradigm: rightward pursuit after an initial saccade to the left

The paradigm starts with an initial fixation period of the central target (bottom panel). The different panels represent the epochs of one trial of the direction pursuit paradigm. The arrows in the time slices indicate the direction of target displacement. Filled symbols refer to visible targets (the red LED), open symbols to invisible targets. FP = fixation point, PT = pursuit target.

divided into eight direction sectors (rightward, right-downward etc.). To compare the neuronal activity evoked by the visual stimulation in the different directions, the activity during these temporal intervals was calculated. The analysis windows were shifted by 80 ms to correct for the average visual latency of the neurons. A Kruskal-Wallis analysis of variance was used to test for the effects of the stimulation on the neuronal activity. If the neuron was significantly modulated ($P < 0.05$), the preferred visual direction of the neuron was determined. To do this, the preferred direction per trial was determined on the basis of the activity in the eight analysis windows. The overall preferred direction was computed as the resultant vector of the direction vectors of all trials.

To quantify the direction selectivity we defined a DI analogous to that for pursuit-related direction selectivity.

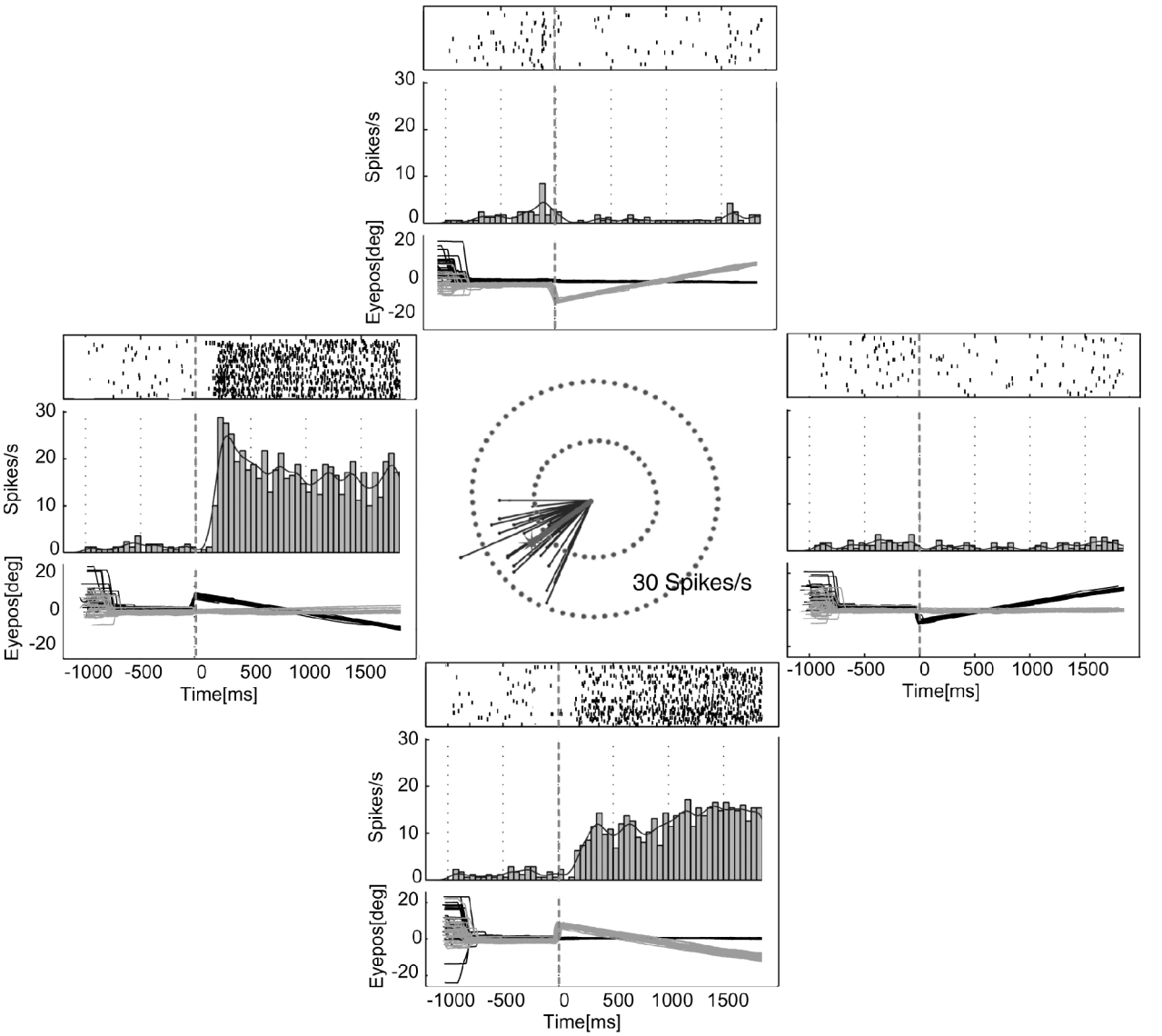

Figure 2. Example of the response of one neuron during the pursuit direction paradigm

The four panels show the activity of the neuron and the corresponding eye positions during upward, leftward, downward and rightward pursuit. All data are aligned to saccade offset. The upper part of each panel consists of a raster plot of the spike times. Each black dot represents one spike event and each row of dots one trial. The dashed line refers to the time of saccade offset. The middle part of each panel shows the mean activity of the neuron in a PSTH (peri-stimulus time histogram). In the PSTHs the mean activity across trials has been computed by sorting the data into 50 ms bins. The continuous black line represents the spike density function, determined with a fixed kernel of 30 ms by a standard protocol as described, for example, by Munoz & Wurtz (1993). In the lower part of each panel the eye position is plotted over time. Black lines indicate the horizontal eye position, grey lines the vertical eye position. The polar plot in the centre of the figure represents the direction vectors for each complete set of trials, i.e. computed as the resultant vector of the successive pursuit in all 4 directions. The grey vector indicates the overall preferred direction (PD) of this individual neuron corresponding to PD = 216 deg.

Comparison of the visual preferred direction with the pursuit preferred direction. For neurons that were direction selective during both the visual stimulation and the pursuit direction paradigms, we computed the differences in the preferred directions in the two conditions by subtracting the visual preferred direction from the pursuit preferred direction. Accordingly, for example, a resultant value of '0 deg' would indicate that the neuron preferred the same direction of movement in the two different tasks. A value of '180 deg' would correspond to opposite directional tuning in the two conditions. For each of these neurons we determined the confidence intervals for the visual and pursuit preferred directions. This allowed us to test whether the two preferred directions were significantly different.

Influence of the 'blink period' on eye velocity and neuronal activity. To determine the influence of the blink period on eye velocity and neuronal activity, the eye position and neuronal data were aligned to the onset of the blink. We determined the eye velocity and neuronal activity during three time periods: the period before, during and after the blink for each trial.

For eye velocity, the first analysis window lasted from 500 ms before to the onset of the blink. The influence of the extinguished target on the eye velocity would only appear after a certain neuronal processing time during which the change in visual information would be translated into a change in the motor command. We thus determined the eye velocity for the blink period during a 100 ms window from 150 ms after the onset of the blink to 50 ms after the reappearance of the pursuit target. If the blink period had an effect on the eye velocity, it should be maximal in this time range. The last analysis window, which determined the eye velocity after the reappearance of the pursuit target, began 150 ms after the offset of the blink period and ended at the end of the trial.

The first window for the calculation of neuronal activity was the same as for the eye velocity analysis. The second window began 80 ms after the onset of the blink period, to correct for visual latencies, and lasted until 80 ms after the offset of the blink. The time remaining until the end of the trial comprised the last analysis window.

To test for significant influences of the blink period on eye velocity and neuronal activity, we performed a Kruskal-Wallis analysis of variance. For neurons with significant differences in either eye velocity or neuronal activity, we determined whether these differences were caused by a decrease in the values during the second window in comparison to the first window ('a dip').

RESULTS

Direction paradigm

We recorded from 234 neurons in area VIP of two monkeys performing the pursuit task; 123 of the neurons (i.e. 52.6 %) showed a significant tuning of their activity for the direction of the pursuit eye movement. The mean DI across all direction-tuned neurons was 0.44 (± 0.01) indicating that on average the neurons' discharge during SPEMs in the preferred direction was nearly twice as high as the discharge during SPEMs in the null direction. However, the strength of direction selectivity for the SPEMs was notably less than that for visual motion stimulation (mean DI 0.79 ± 0.01). An example of a neuron tuned to the direction of the pursuit eye movement is shown in Fig. 2.

Figure 3 shows the distribution of preferred pursuit directions of the 123 direction-selective neurons. Since we recorded from the left hemisphere in the first monkey and the right hemisphere in the second monkey, the data from the second monkey were mirrored with respect to the vertical meridian for the analysis of the distribution of preferred directions. This procedure allowed us to distinguish between ipsiversive ('ipsi') pursuit, i.e. the direction toward the hemisphere that was recorded from, and contraversive ('contra') pursuit, i.e. the direction away from the recording side, rather than leftward and rightward pursuit. We determined the distribution of preferred directions within the four sectors 'up', 'ipsi', 'down' and 'contra' (separated by the grey dashed lines in Fig. 3) and performed a χ^2 test to discover whether the observed distribution was different from a uniform distribution. There was no significant bias for any of the four sectors ($P = 0.12$, 3 DF).

The mean latency of the postsaccadic pursuit relative to target onset was 210 ± 13 ms in the first animal and 230 ± 6 ms in the second animal. Relative to saccade offset, i.e. to the start of the post-saccadic pursuit, neuronal discharge had on average a latency of 266 ± 16.71 ms in the first and 160 ± 11.51 ms in the second animal.

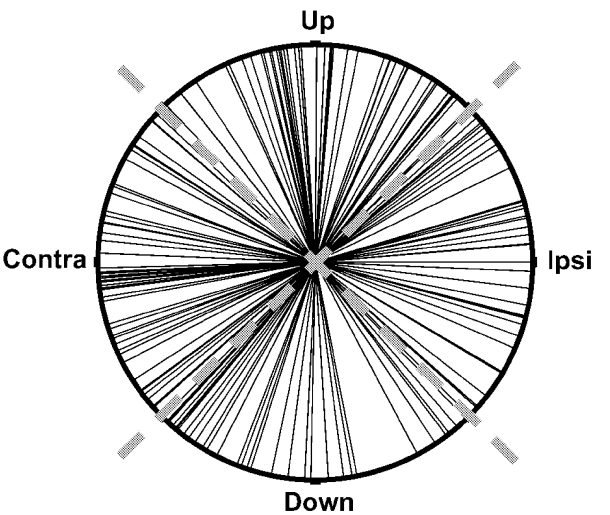

Figure 3. Distribution of preferred pursuit directions (*n* = 123)

The figure shows the preferred pursuit directions of the 123 direction-selective neurons. Data from the first monkey have been mirrored with respect to the vertical axis. Vectors pointing to the left thus indicate a contraversive preferred direction ('contra') and rightward pointing vectors an ipsiversive preferred pursuit direction ('ipsi'). The preferred directions were divided into four 90 deg sectors whose limits are indicated by the dashed grey lines. See text for details.

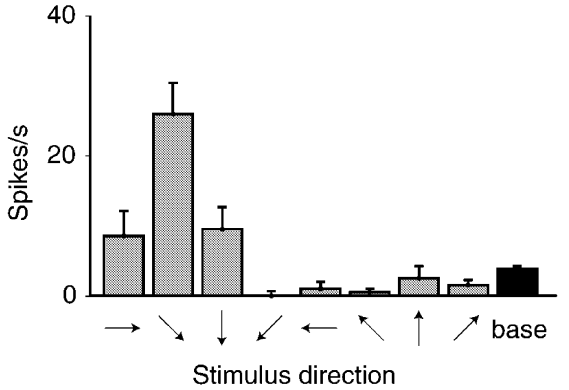

Figure 4. Visual direction tuning of the example neuron shown in Fig. 2

The grey bars show the mean spike activity (+ standard error) of the neuron during visual stimulation in different directions. The arrows below the *x*-axis depict the respective motion directions of the visual stimulus. The black bar ('base') shows the mean baseline spike rate (+ standard error) of the neuron. The activity of the neuron was highest during downward and rightward directed visual motion. The preferred visual motion direction of this neuron was 321 deg.

We performed two different types of analyses to determine whether this pursuit-related activity depended on visual signals: (i) we compared the relationship between the visual and the pursuit preferred direction and (ii) we analysed neuronal activity and eye movements during the blink period.

Comparison between visual and pursuit preferred directions

We recorded from 205 neurons during both the pursuit direction paradigms and the visual stimulation task.

One hundred and twenty three of these neurons (60 %) were significantly tuned to the pursuit direction, whereas 164 (80 %) were direction selective for the visual stimulation. Ninety-five neurons (46.3 %) had a significant directional tuning in both conditions. For the latter group of neurons the difference in preferred directions was determined.

The neuron shown in Fig. 2 had a preferred pursuit direction of 216 deg, i.e. its discharge was strongest during leftward and downward directed pursuit eye movements. The corresponding response of this neuron to visual stimulation is shown in Fig. 4. The neuron's visual preferred direction was 321 deg, i. e. down and to the right. The difference between the visual and pursuit preferred direction of this neuron was thus 105 deg. Considering the confidence intervals for both visual and pursuit preferred directions, this difference was significant ($P < 0.05$).

Figure 5 shows the distribution of differences between preferred pursuit and visual directions for the 95 neurons with significant directional tuning in both conditions. The differences covered the whole possible range between 0 and 360 deg. We divided this range in four 90 deg sectors as indicated by the dashed grey lines in the polar plot of Fig. 5. The distribution of differences among these four sectors was significantly different from a uniform distribution ($P < 0.001$ χ^2 test). For 82 % of the neurons (78/95) the PDs in the pursuit direction paradigm and the visual stimulation task were opposite (44/95) or either 90 or 270 deg off (34/95). Since the background was completely dark, at least for this sample of neurons the pursuit activity cannot be caused by visual signals. Only for 18 % of the neurons (17/95) did both PDs coincide. For these neurons with the smallest directional differences (difference < ±45 deg) the question remains unanswered of whether or not the activity during the pursuit task was caused by visual signals, i.e. the retinal slip of the pursuit target.

Blink analysis

We performed the blink analysis for all cells with pursuit-related responses ($n = 123$). The blink period had an

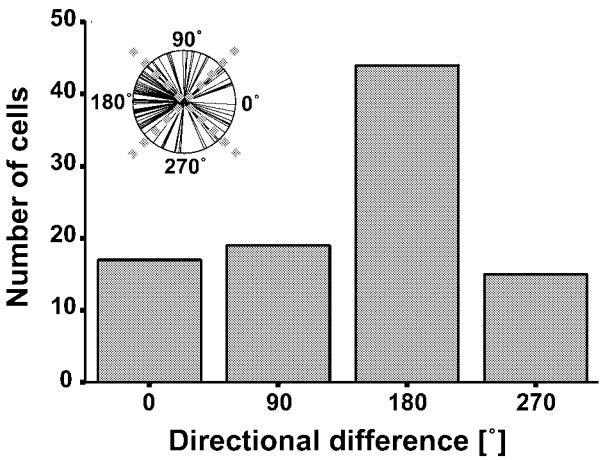

Figure 5. Distribution of differences between the visual and pursuit preferred direction (n = 95)

The polar plot in the upper left corner shows the raw distribution of the direction differences. Each line represents the direction difference for one neuron. Neurons with the same preferred direction in both tasks, i.e. 0 deg difference between the respective preferred directions, are represented by vectors to the right. Neurons with opposite directional tuning, i.e. a 180 deg difference between the two preferred directions, are represented by vectors to the left. Vectors pointing upward or downward indicate differences of 90 deg or 270 deg, respectively. The bar plot summarises these results by dividing the range of possible direction vectors into the 4 sectors, indicated by the dashed grey lines in the polar plot.

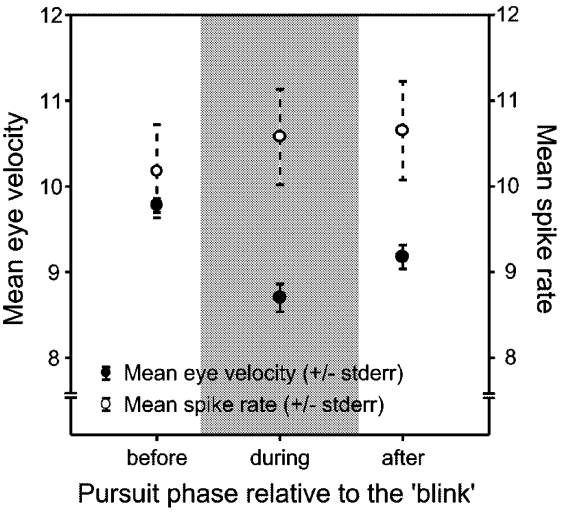

Figure 6. Mean eye velocity and neuronal activity in the periods before, during and after the blink

The target velocity was 10 deg s^{-1} for all three periods. The eye velocity in the three time intervals was averaged over 67 recordings, the spike activity over the 123 neurons with significant pursuit directional tuning. The figure shows these averages ± standard error. The grey area highlights the respective values for the period during the blink. While the mean neuronal activity did not show a decrease, the mean eye velocity was markedly decreased during the blink period in comparison to the values before and after this period.

influence on the eye velocity. During the experiments, sometimes signals from several neurons were recorded simultaneously from a single electrode by means of a spike sorting system (Alpha Omega Inc.). Hence, the number of different eye movement recordings ($n = 67$) is lower than the total number of cells used in this analysis ($n = 123$) but equals the number of recording sites. We analysed the mean eye velocity of these 67 recordings for each pursuit direction (at least six trials per direction). For all directions the eye velocity was significantly lower during the blink period in comparison to the period before and after the blink ($P < 0.001$, Kruskal-Wallis analysis of variance). However, only 29 of the 123 neurons (i.e. 23.6 %) showed a significant decrease of spike activity in at least one (usually the preferred) pursuit direction ($P < 0.05$, Kruskal-Wallis analysis of variance). Figure 6 shows the mean spike rate and the mean eye velocity in the three analysis windows 'before', 'during' and 'after' the blink for all neurons with significant pursuit tuning ($n = 123$). While the mean eye velocity was significantly decreased during the blink period ($P < 0.001$, Kruskal-Wallis analysis of variance), the mean spike rate was not reduced with respect to the pre-blink interval ($P > 0.05$, Kruskal-Wallis analysis of variance) but rather slightly (but non-significantly) enhanced.

Both analyses delineated in this section, i.e. the comparison between visual and pursuit preferred directions and the blink analysis revealed neurons for which the respective criteria for a putative visually driven pursuit response were fulfilled. For these neurons, pursuit-related activity could be simply explained by pursuit-induced visual motion on the retina. The question arises of whether or not neurons exist for which the simple visual explanation would apply in both cases. Therefore, the blink analysis was performed again for the 17 neurons with a direction difference of 0 deg found in the first analysis. Only two of these neurons showed a significant decrease in pursuit activity in at least one condition ($P < 0.05$). Hence,

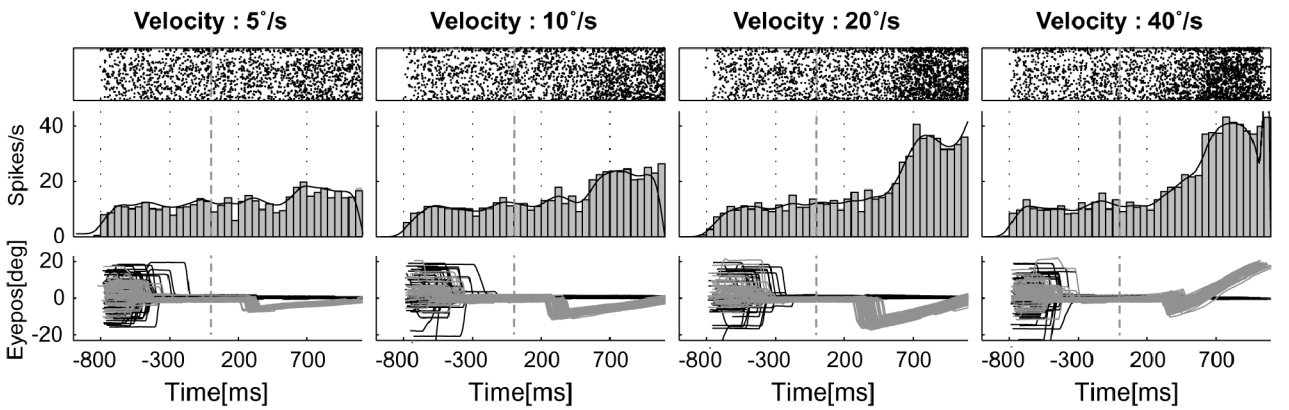

Figure 7. Example of the response of a single neuron to upward pursuit with different velocities

Same conventions as in Fig. 2. In this figure the data are aligned to target onset (grey dashed line) to show the variability in saccade latency. The velocity tuning of this neuron is described in more detail in Fig. 8.

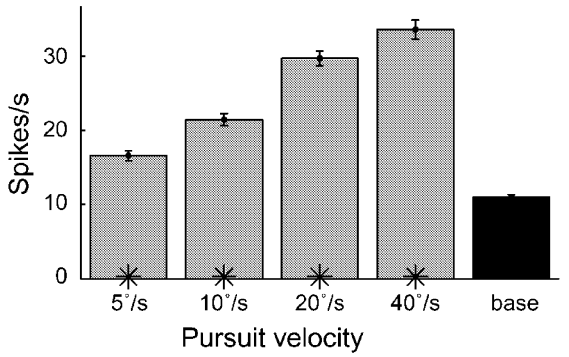

Figure 8. Mean rate during the pursuit phases with the different velocities in comparison to the baseline activity

Mean activity (± standard error) was calculated during the pursuit phase for each velocity across trials for the same neuron as in Fig. 7. The level of baseline activity (computed as the mean activity during fixation) is given by the black bar. The Kruskal-Wallis analysis revealed significant modulation of the neuron by the pursuit paradigm. The *post hoc* tests showed that the activity of the pursuit phases for all velocities were significantly different from baseline activity (indicated by the black stars). The discharge of this neuron was highest for the pursuit velocity of 40 deg s^{-1}, i.e. it preferred the highest velocity applied.

for only 2 % of the neurons that were direction selective during pursuit could this activity be based on simple visual factors.

Velocity paradigm

In this paradigm the monkey had to perform SPEMs with different velocities. The gain of the eye movement dropped only slightly with increasing pursuit velocity. The mean gain of the pursuit phase was 0.96 for SPEMs with 5 deg s^{-1}, 0.93 for SPEMs with 10 deg s^{-1}, 0.89 for SPEMs with 20 deg s^{-1} and 0.85 for SPEMs with 40 deg s^{-1}.

We recorded from 87 neurons during this velocity paradigm. Sixty-four of the 87 neurons (i.e. 73.6 %) had a significant velocity tuning ($P < 0.05$). An example of the velocity tuning of one neuron is shown in Figs 7 and 8. The neuron that is depicted in these figures preferred upward pursuit with the highest velocity applied (40 deg s^{-1}).

We determined the preferred velocity for all 64 velocity-tuned neurons and computed the number of neurons preferring a particular pursuit velocity. The distribution of the preferred velocities is shown in Fig. 9. There was a significant preference for high pursuit velocities (χ^2 test: $P < 0.001$), i.e. 85.9 % of the neurons had their response maximum at the peak velocity (40 deg s^{-1}).

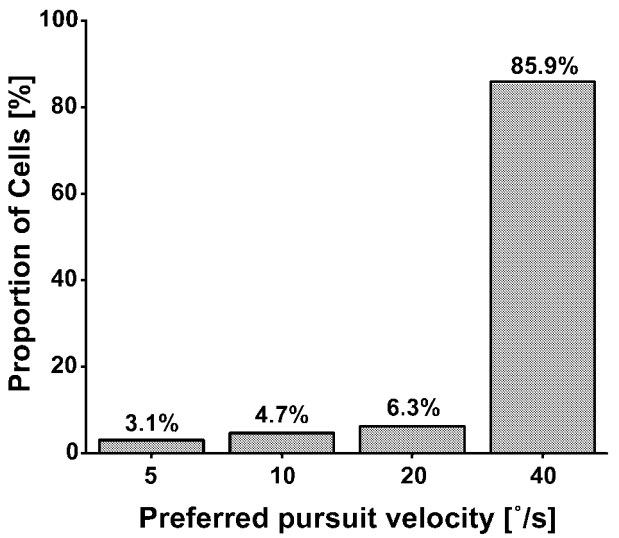

Figure 9. Distribution of preferred velocities among the population of 64 significant velocity tuned neurons

The distribution of preferred velocities was significantly different from a uniform distribution ($P < 0.001$, χ^2 test). Most neurons' discharge was strongest during the highest pursuit velocity of 40 deg s^{-1}.

DISCUSSION

Pursuit-related activity in area VIP and its dependency on pursuit parameters

The present study describes the activity of 234 neurons in the macaque ventral intraparietal area (area VIP) during SPEMs. 52.6 % of the neurons showed a significant pursuit direction tuning. This is a slightly higher proportion than has been reported in other parietal cortex regions (e.g. 39 % pursuit cells in the dorso-posterior part of area LIP and 42 % in area 7a; Bremmer *et al.* 1997*a*). It is also higher than the proportion of pursuit-related neurons in area MT (35 %: Bremmer *et al.* 1997*c*, 31 %: Komatsu & Wurtz 1988), which projects to area VIP. In area MST, which is also highly interconnected with area VIP, the proportion of neurons exhibiting direction-selective responses to step ramp pursuit eye movements appears to be within the range found in our study (31 %: Komatsu & Wurtz 1988; 48 %: Bremmer *et al.* 1997*c*). This adds to previously found similarities between the response properties of areas VIP and MST (e.g. Schaafsma & Duysens, 1996).

Distribution of preferred directions

In the present study we show that neurons in area VIP cover the whole range of possible preferred pursuit directions (cf. Fig. 3). A recent study showed that area VIP sends direct projections to the dorsolateral pontine nucleus (DLPN) (Distler *et al.* 2002). The DLPN also receives heavy projections from areas MT and MST (e.g. Maunsell & Van Essen, 1983; Distler *et al.* 2002) and is

involved in pathways from the cortex to the cerebellum and other oculomotor structures important for the generation of SPEMs (e.g. Thier *et al.* 1988; Mustari *et al.* 1988; Kawano *et al.* 1996; Inoue *et al.* 2000). The visual and smooth pursuit-related responses of DLPN neurons like those of areas VIP, MT and MST cover the whole range of possible preferred directions (e.g. Komatsu & Wurtz, 1988; Mustari *et al.* 1988; Thier *et al.* 1988; Suzuki *et al.* 1990). Despite these similarities, it is not very likely that area VIP is directly involved in the generation of SPEMs. One main reason for this assumption is that the pursuit-related activity observed in our study exclusively occurred after the onset of the SPEMs. During eye movements like SPEMs, the image on our retinae changes, although the environment projected onto the retinae does not necessarily change. It has been proposed that the brain might solve the problem of creating a stable percept of the environment across eye movements by using extraretinal signals. These hypothesised signals have been termed 'corollary discharge' (Sperry, 1950) or 'efference copy' (von Holst & Mittelstaedt, 1950; for review see e.g. Bremmer & Krekelberg, 2003). Such information could be used to subtract the signals due to the movement of the eyes from the actual motion on the retinae and in turn to create a representation of the external world independent of eye movements. Accordingly, it is more likely that the SPEM-related activity of area VIP neurons is used to process the sensory consequences of SPEMs.

Velocity tuning

In the present study, we show that neurons in area VIP have a clear preference for high pursuit velocities (86 % of the neurons preferred the pursuit velocity of 40 deg s^{-1} (χ^2 test: $P < 0.001$; see Fig. 9). Since the tracking phases were centred on the screen for all velocities, a possible modulation of cell activity caused by eye position effects could not account for the selectivity observed. One other possible explanation for the preference for high pursuit velocities is related to the known preference for high velocities of visual stimuli (Bremmer *et al.* 1997*b*). However, the pursuit experiments described in the present study were performed in a dark room. The only visual stimulus consisted of the small pursuit target. Different velocities of the pursuit targets on the retina could only occur if the monkey was not able to maintain a high gain during the steady state pursuit phase. The upper limit of smooth pursuit for humans is 100 deg s^{-1} (Meyer *et al.* 1985), the limit for monkeys is even higher (for review see Ilg, 1997). The pursuit velocities used in the present study are therefore not within the range of eye velocities in which the task begins to be really difficult for the monkey (the highest pursuit velocity used was 40 deg s^{-1}). Likewise, the gain of the SPEMs did not vary substantially between the four different pursuit velocities, indicating that the monkey was able to perform the task very well. Since the visual velocity tuning of area VIP neurons is rather broad (Colby *et al.* 1993), the minor changes in retinal slip velocity cannot account for the large changes in cell activity shown in this study.

High retinal velocities are commonly induced by objects moving in near rather than far space. Area VIP has been shown to have a predominant representation of near space, i.e. the action space for head movements (Colby *et al.* 1993; Bremmer & Kubischik, 1999; Bremmer *et al.* 2001, 2002*a*,*b*). The most likely explanation for the observed preference for high velocity pursuit is therefore linked to this biased representation of objects in near space. On the basis of this finding, it would be very interesting to perform additional experiments in which the pursuit activity of area VIP neurons during pursuit of targets at different depths is compared.

Visual *vs.* extraretinal information

To determine whether the pursuit-related activity found in area VIP was related to sensory processing or to oculomotor signals, we used two criteria. We first performed an analysis in which the preferred direction during pursuit was compared to the visual PD. The experiments were performed in darkness and the lights were switched on prior to a new set of trials to avoid dark adaptation of the monkey. Under natural conditions, however, pursuit of a target results in an additional visual stimulation caused by the background. The combination of pursuit in one direction with a background motion into the opposite direction is thus the most frequent combination occurring during SPEMs outside the laboratory. This could be the reason for the finding that nearly half of the neurons in our study showed an opposite directional tuning for visual motion and SPEMs (see Fig. 5). In addition, our results are similar to the findings of Sakata and colleagues, who showed, that nearly half of the neurons in area 7a with pursuit-related discharges show such an anti-directional behaviour (Sakata *et al.* 1983). In our study the difference in preferred directions of the remaining neurons was uniformly distributed over the whole possible range. This broad range of combinations of preferred directions in the two tasks indicates that, at least for a portion of the neurons, visual responsiveness could not account for the directional tuning in the pursuit paradigm. For only 18 % of the neurons did the visual and pursuit PDs coincide, so that visual stimulation caused by retinal slip of the target could have accounted for the observed pursuit-related activity. Nevertheless we performed an additional analysis to test whether the activity found could be related to visual signals: we tested whether extinguishing the target for a 200 ms blink period had an influence on the neuronal activity. Only 23.5 % of the neurons showed a significant decrease in spike activity during the blink period, while the activity of the remaining neurons remained stable or even increased slightly (see Fig. 6). During the blink period visual retinal slip

information was absent. The activity of the neurons with reduced activity during the blink period may therefore be linked to the missing visual information. However, as has already been shown in other studies before, and in the present experiments, the blink always caused a reduction in eye velocity (Becker & Fuchs, 1985; Ilg & Thier, 1997). The drop in neuronal activity that we observed in some neurons could be caused by extraretinal information about eye velocity. Hence, both tests performed to determine whether the pursuit activity in area VIP is related to visual or extraretinal factors indicate that a large number of neurons encode extraretinal information, although we cannot rule out the possibility that a small number of neurons are sensitive to more visual aspects of SPEMs. However, only 2 % of all neurons fulfilled both criteria for a visually based pursuit activity, i.e. they showed a decrease in spike activity during the blink and had a difference between the visual and pursuit preferred directions of 0 deg. Hence, it appears that for the vast majority of neurons in area VIP pursuit-related activity is provided by extraretinal signals.

While neurons in area MT have been shown to encode the visual retinal slip information, area MST combines visual with extraretinal factors and can therefore encode target movement in space (Newsome *et al.* 1988; Thier & Erickson, 1992; Erickson & Thier, 1992; Ilg & Thier, 1997). Similar to the present results in area VIP, there are many neurons in area MSTd that have opposite preferred directions of visual and pursuit-related activity, i.e. the encoding of visual motion and pursuit direction are synergistic (Komatsu & Wurtz, 1988). Area VIP and area MST are highly interconnected and both receive input from area MT (e.g. Lewis & Van Essen, 2000; Van Essen *et al.* 1981). The pursuit-related activity in area VIP may therefore, similar to that in area MST, be used to generate a stable percept of target movement in head-centred space (Duhamel *et al.* 1997).

Conclusion

Area VIP is thought to play a role in the coordination of head movements such as reaching with the mouth for objects or obstacle avoidance. The preference for high velocity pursuit shown in the present study is in line with this suggestion. For the generation of such head movements it is crucial to have access to information about one's own motion and the position and movement direction of objects in space. The current study shows that neurons in area VIP represent both visual motion information and information about the SPEMs, i.e. direction and velocity information, with no fixed relation to each other. The signals in this area could therefore be used to subtract the motion on the retina caused by the actual eye movement from the external motion and create a representation of target position and movement in relation to the head. This representation could then be used for the generation of head movements such as grasping something with the mouth or avoiding contact with an obstacle.

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Acknowledgements

This work was supported by grants from the Deutsche Forschungsgemeinschaft (SFB 509/B7). Special thanks to Claudia Distler for help with surgery and histological analysis of the recording sites.

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