Area MST and Heading Perception in Macaque Monkeys

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The macaque medial superior temporal area (MST) is proposed to be specialized for analyzing complex 'optic flow' information. Such space-varying motion patterns provide a rich source of information about self motion, scene structure and object shape. We report the performance of rhesus macaques on a two-alternative 'heading' task, in which they reported whether horizontally varying, simulated trajectories were to left or right of center. Monkeys were sensitive to small heading angles; thresholds averaged 1.5–3°. Heading estimates were stable in the face of changing stimulus location and smooth pursuit eye movements. In addition, we tested the role of area MST in heading judgements by electrically activating columns of neurons in this area while the monkeys performed the heading task. Activation of MST frequently affected performance, usually causing choice biases. These induced biases were often large and usually concordant with the preference of the neurons being activated. In addition, the induced biases were often larger in the presence of smooth pursuit eye movements. These results favor the hypothesis that MST is involved in recovering self-motion direction from optic flow cues and in the process by which heading perception is compensated for ongoing eye movements.

Introduction

The estimation of self-motion from visual cues is an essential component of navigation through the environment. Gibson (Gibson, 1950) defined optic flow as the complex, space-varying motion patterns produced by observer motion through visual scenes. Psychophysical experiments show that humans are extremely good at recovering the direction of heading from patterns of optic flow, even without any actual self motion. Subjects can resolve their direction of motion from random dot displays with a precision of ~1–3° (Warren, 1998). Furthermore, subjects can largely compensate for ongoing smooth pursuit eye movements, which would degrade the retinal flow-field information if left uncompensated (Warren and Hannon, 1990; Royden *et al.*, 1992, 1994). Despite disputes over exactly which cues are utilized for this compensation, it appears that 'extraretinal' (e.g. oculomotor efference copy or proprioceptive feedback) signals of ongoing eye movements are used under many circumstances.

Electrophysiological experiments on the 'motion system' of dorsal extrastriate cortex in monkeys have identified cortical areas that might be involved both in analyzing complex optic flow information and in compensating this information for ongoing pursuit eye movements. Although it is not the only area representing such information, MST is one promising candidate. Cells in this region have large receptive fields and many are highly selective for particular optic flow patterns, such as expansion, contraction, or rotation (Saito *et al.*, 1986; Tanaka *et al.*, 1986; Duffy and Wurtz, 1991, 1995, 1997). Such components are present in the optic flow patterns produced by self-motion through normal scenes (Koenderink, 1986; Koenderink and van Doorn, 1987). Indeed, MST cells are often selective for particular

headings (Bradley *et al.*, 1996; Duffy and Wurtz, 1997) and their responses are at least partially compensated for smooth pursuit eye movements (Bradley *et al.*, 1996). These features suggest that MST may be a substrate for the recovery of heading from optic flow information.

To test the hypothesis that macaque MST is involved in heading tasks, we trained two monkeys to discriminate their perceived heading from random dot patterns simulating trajectories toward three-dimensional clouds. Here we report that the perceptual performance of monkeys on this task appears to resemble that of human subjects on similar tasks. Furthermore, we tested the involvement of area MST by using electrical microstimulation to perturb its activity during task performance. The general approach is similar to that used in other experiments testing the role of MT and MST in the perception of translational dot motion (Salzman *et al.*, 1992; Celebrini and Newsome, 1994b). In our experiment, we applied microstimulation during smooth pursuit eye movements or during fixation. When applied to a region of MST preferring one heading alternative, microstimulation frequently induced biases, which correlated well with the heading preferences of neurons at the stimulation site. In addition, bias frequently depended on the pursuit condition. This pattern of results supports the hypothesis that MST is involved in recovering self-motion from optic flow and compensating heading perception for pursuit eye movements.

Parts of this work have appeared in short form (Britten and van Wezel, 1998). This paper additionally analyzes the normal psychophysics of our monkey subjects and relates stimulation site tuning to the effects of microstimulation.

Materials and Methods

Subjects and Surgery

Two female rhesus macaques (*Macaca mulatta*) were used in this study. Each was implanted with a head restraint post and a scleral search coil following the previously described method (Judge *et al.*, 1980). The hardware was implanted under surgical anesthesia using sterile techniques in a dedicated primate surgical suite (California Regional Primate Research Center, UC Davis). After several months of training on the psychophysical task, each monkey was additionally implanted with a chronic recording cylinder over occipital cortex. This cylinder (Crist Instruments Inc.) was oriented parasaggitally, 17 mm lateral to the mid-saggital plane and elevated 20° above the horizontal plane, allowing posterior access to extrastriate cortex in the superior temporal sulcus. All animal procedures were approved by the UC Davis Animal Care and Use Committee and fully conformed to ILAR and USDA guidelines for the treatment of experimental animals.

Task and Stimulus

The monkeys were initially trained to fixate small targets on a CRT screen and make saccades to eccentric targets, and then trained on the heading discrimination task. The task was a two-alternative forced-choice task in which the monkeys discriminated between headings to the left or right of dead ahead (Fig. 1). The stimulus simulated a linear 'virtual trajectory'
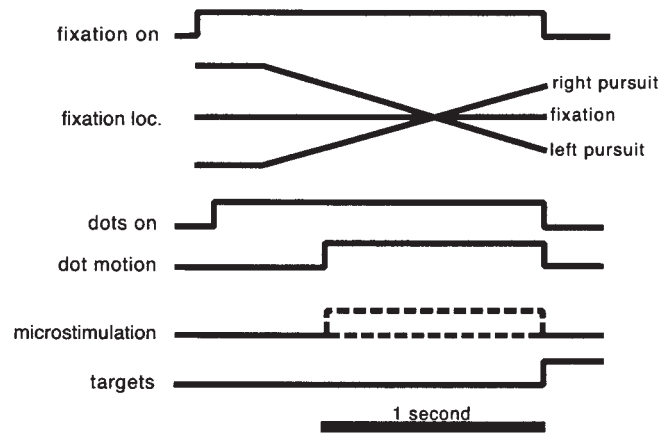
A. top view
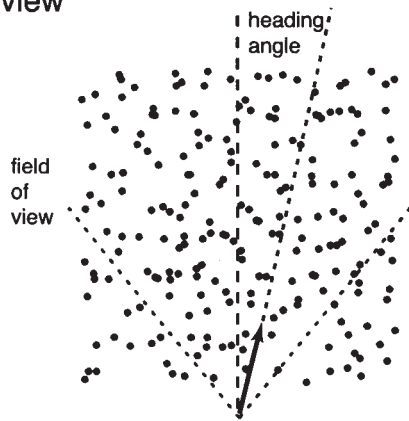
B. timing

Figure 1. Stimulus schematic and task timing. (*A*) Top view of the simulated geometry of the task. The arrow shows the trajectory with respect to the stationary dot fields, which represents a cube in three-dimensional space. The vertical dashed line shows straight ahead and the angled dashed line illustrates the heading angle for the particular trajectory. For reasons of graphical clarity, the illustrated angle is larger than most that were used. The dotted lines indicate the limits of the field of view on the projection on the monitor. (*B*) Timing of events in the task. For the fixation location lines, upward on the page indicates right locations. The two dashed lines for the microstimulation portrayal indicate the two types of trial that are possible—some trials lack microstimulation.

through a three-dimensional cubic cloud of points. Monkeys performed a difference limen task in which the heading angle could be very close to zero. A top view of a representative simulated path (Fig. 1*A*) illustrates depth relationships and relative trajectory length. The simulations corresponded to a trajectory of 1 m toward a cube of points 10 m on a side, centered 5.5 m away, occurring over 1 s. (Other equivalent real-world situations differ by only a scale factor.) Thus, the stimulus contained a large range of simulated depths, which produced a relatively large range of local velocities in the subject's view of the stimulus. The linear trajectory was always left or right of center and the monkey's task was to report which was presented, by making a saccadic eye movement to a subsequently presented target on the same side of the screen. In an individual trial (Fig. 1*B*), the fixation point appeared first and after the monkey fixated it the (stationary) stimulus dots appeared. The fixation point commenced motion 250 ms later if the trial included smooth pursuit; otherwise, it remained at its initial location. Another 250 ms later, the stimulus dots moved, simulating the specified trajectory for the trial. After 1 s of continuous motion, the stimulus dots and fixation point disappeared and two saccade targets appeared. The targets were on the line of possible headings, 8° left and right from dead ahead. Choices to

the correct target were rewarded with a small drop of water or juice; incorrect choices resulted in a brief time-out period. Incomplete trials were discarded from analysis. This trajectory varied along the horizontal plane, specified by a 'heading angle' (Fig. 1*A*), the angle between the simulated trajectory and straight ahead. The center of this range of headings (objective dead ahead) was always at the center of the screen and was thus fixed with respect to the monkey's head. The heading angle was varied during a block of trials from 0.5 or 1° to 8° by factor of two increments, according to the method of constant stimuli. If an animal developed a strong bias toward one or the other alternative, 'correction' trials were presented, with the stimulus fixed in the less-preferred direction. These correction trials were discarded from analysis.

The heading stimuli were generated on a PC using custom software. They consisted of 400 (early experiments) or 2000 black dots, each 0.17° across, on a uniform grey background of 11.3 cd/m². Although the dots' contrast could not be measured accurately due to their small size, it closely approached 100%. The screen was positioned 23 cm from the monkey's eyes, and subtended 80° horizontally by 60° vertically. The room was dimly illuminated and the background was stationary on the screen. The number of dots is unlikely to affect the results, as human psychophysical performance on similar tasks is asymptotic beyond ~10 dots (Warren *et al.*, 1988).

The monkeys were initially trained on easy (for human subjects) versions of the task, with central fixation and large heading angles. They learned the basic task rapidly, typically within two sessions. Next, smaller heading angles were included, until the animals' psychometric functions allowed us to estimate their heading thresholds. Next, the monkeys were trained to generalize across a range of fixation locations and to report heading during pursuit eye movements. Lastly, the monkeys were presented different conditions in rapid alternation, emulating experimental conditions. When thresholds were asymptotically low, monkeys were deemed ready for the stimulation experiment.

Recording and Stimulation

Monkeys were seated in a primate chair with their heads restrained. Eye movements were measured with a scleral search coil system (David Northmore Inc.) and sent to a PC running the public domain experimental control software REX (Hays *et al.*, 1982). On recording days, the cap covering the cylinder was removed and an electrode (glass-insulated Pt–Ir, 0.5–1.0 MΩ, FHC Inc.) was introduced into occipital cortex via a transdural guide tube. Initial mapping penetrations located the superior temporal sulcus (STS) and identified approximate boundaries of the motion-sensitive areas in its depths. MST was identified according to previously published methods (Celebrini and Newsome, 1994a). To identify the STS, we used a combination of anatomical and physiological landmarks, including the depth from the brain surface, grey matter/white matter transitions, sulcus crossings and response properties. Within the STS, we located and mapped MT on the posterior bank, using its well-understood and consistent retinotopy and responses for physiological confirmation. MST was encountered after crossing the STS to its anterior bank and was identified by large RFs that often included the fovea or extended substantially into the ipsilateral hemifield. In addition, cells on the anterior bank often showed MST-like stimulus selectivities, preferring rapidly moving stimuli and complex optic flow stimuli. All experiments reported here came from penetrations in which the lumen of the STS was crossed and thus most likely from the dorsal subdivision (MSTd). Furthermore, the neurons we recorded typically preferred large stimuli over smaller ones, a hallmark of MSTd. Histological verification of recording sites has not yet been obtained, as both monkeys are still being used in related experiments.

Heading selectivity was measured for multiunit sites at ~100 μm intervals. When a region of clear and consistent heading selectivity was found, quantitative heading-tuning measurements were made at more frequent intervals. Sites were deemed acceptable if they maintained clear and consistent selectivity for a distance of 250 μm or more. The electrode was then positioned in the middle of this region and the microstimulation experiment initiated.

The receptive field of each site was established using a mixture of hand- and computer-presented stimuli. The fixation point was adjusted to bring the center of the range of headings into the receptive field and then to maximize heading selectivity. The site's tuning to heading stimuli was

then measured under the pursuit conditions used in the stimulation experiment. A range of headings was chosen to span the expected threshold at that location. During the experiment, a block of trials containing 15 or 20 trials for each condition, was presented. Typically, there were eight or 10 heading angles, three pursuit conditions and two microstimulation conditions, presented interleaved in a fully crossed, block-random design.

The microstimulation consisted of 200 Hz pulse trains delivered through the recording electrode from a multichannel pulse generator (AMPI) and linear stimulus isolator (FHC Inc.). Pulses were biphasic, 20 μA in amplitude, cathodal leading. Each phase was 200 μs in duration, and 100 μs intervened between phases. The pulse train was 1 s in duration, exactly simultaneous with the visual stimulus motion upon which the monkey's decision was based.

Data Analysis

Psychophysical performance was measured both with and without microstimulation, and all resulting psychometric functions were similarly treated. Data consisted of the proportion of rightward choices as a function of heading angle (distance of the simulated heading from straight ahead). Such functions were fit with probit functions (cumulative Gaussians) expressed as follows:

$$P(r) = \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{h} e^{\frac{-(x-u)^2}{2\sigma^2}} \, dx \qquad (1)$$

In this expression, $P(r)$ is the proportion of rightward choices, h is the heading angle, μ is the mean of the Gaussian and σ is the standard deviation or width. The data were fit with an iterative method called 'Stepit' (Chandler, 1965) using maximum-likelihood fitting, assuming binomially distributed choices. In this application, the mean (μ) estimates the bias of the monkey and is zero if the monkey's subjective 'dead ahead' point is veridically in the center of the screen. The width parameter (σ) captures the monkey's sensitivity to heading and is the heading angle required to support 84% correct performance. For the psychophysical data (without microstimulation), each individual function (from the three interleaved pursuit conditions) was fit separately. This approach does not allow statistical testing of individual effects, but provides a simple, unbiased estimate of the fit parameters across the range of conditions tested, which was all we desired to extract from these data.

For the microstimulation and pursuit data, the probit model was elaborated to include additional terms, so that we could test the significance of effects on an experiment-by-experiment basis. If we simplify the above expression (1) as probit(μ,σ), then for any microstimulation condition, $i(0,1)$ and pursuit condition $j(0,1,2)$, we get:

$$P_{i,j}(r) = \text{probit}(\mu + \mu_i + \mu_j + \mu_{ij}, \sigma + \sigma_i + \sigma_j + \sigma_{ij}) \qquad (2)$$

where the single-subscript terms describe the main effects of pursuit or microstimulation and the double-subscript terms describe interaction effects. The significance of these additional terms was tested using likelihood-ratio testing, as described in the text.

Results

Psychophysical Performance

Heading performance has been extensively studied in humans, but little described in monkeys. We measured heading discrimination in two adult female monkeys during their last month of training. During this period, the monkeys' measured thresholds were asymptotically low, with no trend toward improved performance. Thresholds were measured in half-hour blocks of trials, consisting of 24–30 conditions and 15 trials per condition. In each block, heading eccentricity (distance in degrees from fixation point to the center of the range of headings) was held constant and three different pursuit conditions were used – left, right and no pursuit. All conditions were pseudorandomly interleaved.

In humans, sensitivity is largely invariant to heading eccentricity across a range from 0 to ~30° (Crowell and Banks, 1993).
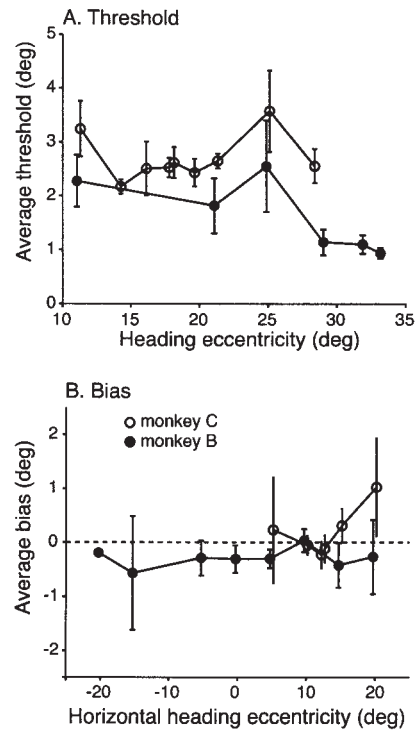

Figure 2. Dependence of heading threshold and bias on heading eccentricity. Heading eccentricity is defined as the distance between the fixation point (or center of pursuit sweep if pursuit is included on the trial) and the center of headings, which was directly ahead of the monkey, in the center of the screen. Sensitivity is estimated by the sigma parameter from the best-fit probit function. For both panels, data were taken from the trials in which the fixation point remained stationary. (*A*) Thresholds did not depend on eccentricity. The weak and inconsistent trends seen in each monkey's data were probably the result of unequal training in different locations and were not statistically significant. (*B*) Bias, estimated from the mean of the best-fit probit function, did not systematically depend on the horizontal heading eccentricity. Monkey C (open circles) was only trained for fixation points to the left of the center of headings.

We found a similar result in monkeys (Fig. 2*A*). Monkey C (open circles) showed reliably higher average thresholds (σ from probit fits) than monkey B ($t = 4.4$, $P < 0.0001$), but in neither animal was the relationship with eccentricity statistically significant (linear regression; monkey C, $P > 0.17$; monkey B, $P > 0.45$). Heading thresholds, therefore, were consistent across our range of eccentricities.

One might expect bias to depend on heading eccentricity and especially on the horizontal component, because distribution of horizontal motion in the image is a profound cue to horizontally varying headings – leftward headings increase the amount of rightward motion and vice versa. If the monkey uses simple, local cues to perform the task, this one would probably be most salient. In this case, we might find biases in our horizontal heading task related to horizontal heading eccentricity. However, no such relationship was apparent in our data (Fig. 2*B*); the average bias remained near zero throughout the range tested. This result occurred for both monkeys tested individually and no relationship was observed with vertical or total eccentricity.

Horizontal retinal image flow is also influenced by horizontal smooth pursuit eye movements, so we measured their effects on bias and sensitivity. As did the variation of heading eccentricity, including pursuit encouraged our monkeys to attend to more global cues and not make a local direction judgement. Because we wished to investigate how microstimulation interacted with pursuit (see below), we needed baseline information on

responses during pursuit. Smooth pursuit produced subtle influences on performance, with substantial day-to-day variation. Both monkeys showed a slight decline in sensitivity under pursuit, with thresholds rising ~10% during pursuit at 10°/s (Fig. 3). This decline was significant by ANOVA [$F(338,2) = 2.803$, $P < 0.05$], as was the difference between monkeys [$F(338,1) = 125.6$, $P < 0.001$]. In both monkeys, threshold declined equivalently for either direction of pursuit.

We also investigated the relationship between bias and smooth pursuit, and used a shift metric to capture induced bias from pursuit (Fig. 4). The curve representing trials with left pursuit (dashed) is shifted to the right with respect to the other two curves, which are essentially identical. Thus, under left pursuit, the monkey made more left choices, as expected from undercompensation for retinal effects of eye movements. The reasons are somewhat counterintuitive. Horizontal pursuit produces retinal image motion opposite the pursuit direction.
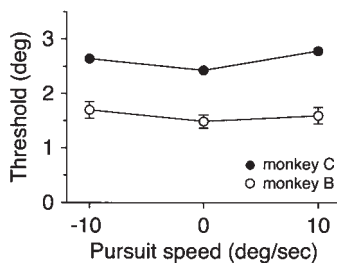

Figure 3. Dependence of threshold (sigma) on pursuit for each monkey. While the monkey was trained on a range of pursuit speeds, most experiments were carried out using a pursuit speed of 10°/s. This speed slightly reduced the sensitivity to heading for both monkeys, but this difference was modest. Where error bars are not visible, they are within the dimensions of the plot symbol.
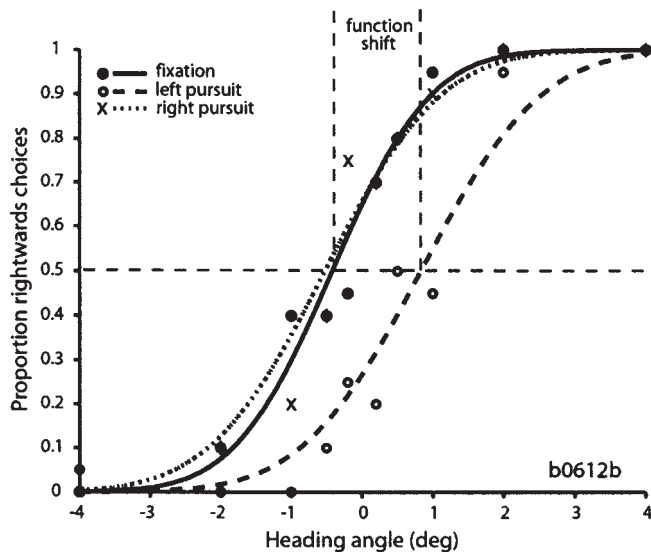

Figure 4. A single experiment in which pursuit influenced heading perception. Data resulting from the three pursuit conditions are illustrated by the three different symbols: solid circles denote fixation, open circles show left pursuit and open diamonds show right pursuit. The three independently fit probit functions are illustrated. To describe the induced bias in such experiments, we measured the horizontal distance between the reference curve (fixation) and each of the others. This shift is graphically depicted by the horizontal distance between the vertical dashed lines, which intersect each curve where it crosses the 50% point (horizontal dashed line). Fit parameters for these functions were as follows: static, $\mu = -0.42$, $\sigma = 1.09$; left pursuit, $\mu = 0.83$, $\sigma = 1.33$; right pursuit, $\mu = -0.53$, $\sigma = 1.29$.

Adding such motion shifts the 'focus of expansion' (normally at the direction of heading) *in the direction of pursuit* (Regan and Beverley, 1982; Duffy and Wurtz, 1997). This, then, produces a bias in the direction of pursuit, if not compensated for in some way. In our experiments, the induced bias was estimated by subtracting the midpoints of fixation and pursuit curves (vertical dashed lines). In the experiment shown (Fig. 4), the shift was just over a degree in magnitude and the effects were asymmetric – right pursuit had little or no effect on performance, unlike left pursuit. Such quirky effects of pursuit upon performance were commonly observed, as shown in the average results (Fig. 5). The two monkeys behaved rather differently. Monkey B (open bars) showed a regular bias to the left under any pursuit condition, whereas monkey C showed biases that depended on pursuit direction. This monkey was biased to the left under right pursuit and to the right under left pursuit. Thus, on average, monkey C tended to slightly overcompensate for the retinal effects of pursuit.

In general, our monkeys' psychophysical performance appeared similar to that of human subjects on similar tasks (Warren and Hannon, 1988, 1990; Royden *et al.*, 1992; Banks *et al.*, 1996), in terms of threshold and effects of eye movements. This lends credence to the idea that the monkeys were performing a true heading task, rather than discriminating some local cue in the stimulus.

Microstimulation Effects

The primary goal of these experiments was to determine the role of area MST in heading perception by perturbing its activity with electrical microstimulation. We first mapped the heading selectivity of multiunit recording sites along oblique penetrations through area MST to find regions of consistent heading selectivity, as MST is organized in a clustered or columnar manner by optic flow preference (Tanaka *et al.*, 1986; Geesaman *et al.*, 1997; Britten, 1998). When a region with consistent heading tuning was identified, we positioned the electrode tip in its center, measured the heading tuning of neurons there and commenced a microstimulation experiment. Figure 6 shows schematically the distance traversed by the electrode with respect to the landmark of the entry into grey matter. The tuning functions below each site show the multiunit tuning for horizontal heading. The hatched region on the penetration denotes the boundaries of the region that showed consistent preference for left headings. This site was ~300 μm in extent, a typical value. The results reported here derive from 67 such experiments, conducted in the same two monkeys whose psychophysical data appear in the previous section. In 16 of
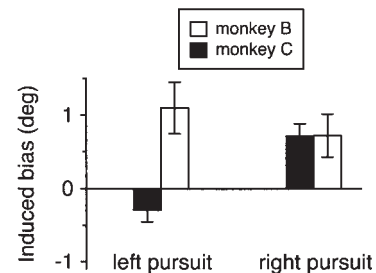

Figure 5. The relationship between pursuit and average induced bias. The induced bias expresses the horizontal shift of the psychometric function under pursuit, compared to that measured under fixation. Both monkeys were largely able to compensate for the distortions in the optic flow produced by pursuit. If uncompensated, the induced bias from the change in retinal optic flow would be ~20°.
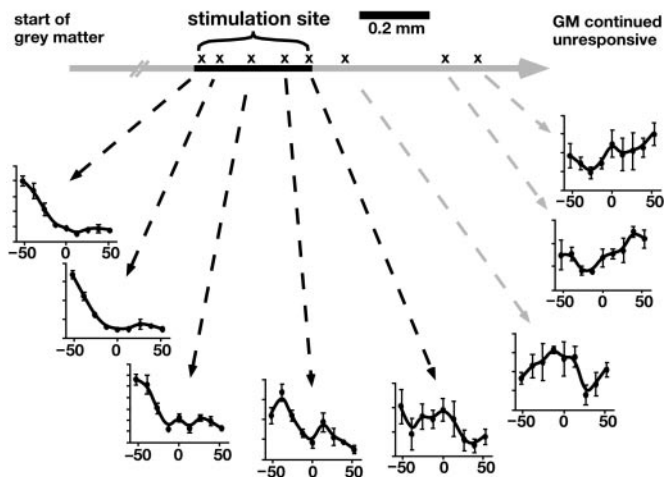
Figure 6. Map of a typical microstimulation site in MST. The Xs mark multiunit recording locations and the corresponding tuning functions show multiunit responses to a range of headings at each site. Vertical scale on each is arbitrary, since the spike threshold could not be set precisely relative to the amplitude of neuronal signals. The bold line on the track record denotes the region in which the tuning was sufficiently clear to pass our criterion and be included in the site.

Figure 7. Example of a typical MST microstimulation experiment. The filled symbols and bold-line curve show performance with microstimulation; open symbols and fine lines depict the interleaved control trials. The site in this case preferred left headings, and microstimulation produced significant decreases in rightwards choices. The best-fit curves were allowed to be fully independent, so that each curve could have its own mean and slope. Nonetheless, the stimulation data are close to a horizontally shifted replica of the control data. Fit parameters for this case were: stimulated, $\mu = -1.58$, $\sigma = 2.47$; control, $\mu = -0.26$, $\sigma = 2.53$.

Figure 8. Effects of MST microstimulation in the absence of smooth pursuit. For each experiment, we calculate the difference in the means (A) and sigmas (B) between the stimulation and control data. For the analysis of bias, the sign of the resulting difference was assigned relative to the preference of the neurons at the stimulation site.

these experiments, we did not include multiple pursuit conditions due to lack of time during the session.

In a typical experiment (Fig. 7), microstimulation lowered the proportion of rightward choices. The results during stimulation consistently lie below the control data, consistent with the preference of neurons at the stimulation site for left headings. In this experiment, the effect on bias was not accompanied by a change in sensitivity; both fit curves had the same slope.

Such changes in bias were frequent in our experiments (Fig. 8A). In this analysis, the sign of the shift was assigned relative to the tuning of neurons at the stimulation site. Shifts that increased choices in the direction of the neurons' preference are depicted as positive; oppositely directed effects are shown as negative. Significant effects (solid bars) were frequent: 28 cases of 67 were individually significant ($P < 0.05$, likelihood ratio test). Interestingly, however, microstimulation biased perception in either direction – not always in the direction predicted by the neurons' preferences. Of significant effects, 18 were in the predicted direction and 10 were in the opposite direction. This proportion of effects, although suggestive of a trend, is not significantly different from chance (binomial test, $P > 0.1$). Furthermore, the mean of this distribution is not significantly different from 0 ($t = 1.6$, $P > 0.5$). Therefore, we can conclude that stimulation frequently, and often substantially, affected the preference of the monkey for heading.

Changes in sensitivity also occurred in these experiments, but were less common. Figure 8B shows the distribution of slope changes seen in the same sample of 67 experiments. Solid bars indicate cases where the change in slope was statistically reliable (10 cases). In this case, there was a reliable trend toward higher thresholds under microstimulation (mean = 0.219, $P < 0.05$). However, the magnitude of the change was small; on average, thresholds changed by only 11%. Two provisional conclusions, then, can be drawn at this point. Microstimulation in MST frequently affected heading perception, both in bias and in sensitivity. The bias effects were often large in magnitude, but unpredictable in sign. The effects on sensitivity were more systematic in sign, but small in magnitude.
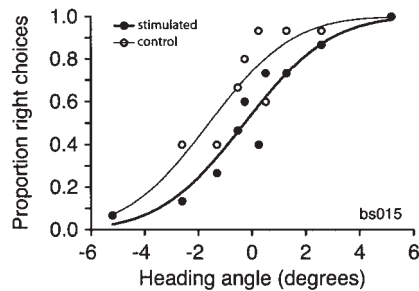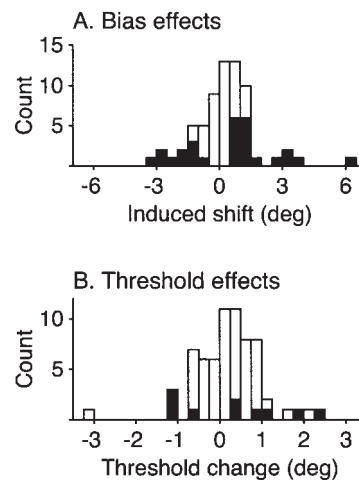
Effects in the Presence of Pursuit

Because of evidence that area MST contains extraretinal signals affecting responses to flow-field stimuli, we were particularly interested in how microstimulation interacted with pursuit (Fig. 9). Each panel shows performance under a different pursuit condition (static, left, or right at 10°/s; microstimulation trials, filled symbols and bold lines). The effect of microstimulation systematically differs, depending on the presence and direction of pursuit: it is modest for the static condition (Fig. 9B), largest for left pursuit (Fig. 9A) and disappears for right pursuit (Fig. 9C).

The full range of possible interactions between pursuit and microstimulation are illustrated as hypothetical examples (Fig. 10). Absent any interaction, the effects of microstimulation in each pursuit condition would be identical (not shown). In Figure 10D, the bias induced by microstimulation is near zero for right pursuit, is modest under fixation and is largest for left pursuit (as seen in the case in Fig. 9). In Figure 10E, the effect of microstimulation on threshold interacts with pursuit. In this case, the threshold for heading is unaffected by microstimulation under left pursuit, is modestly degraded in fixation and is
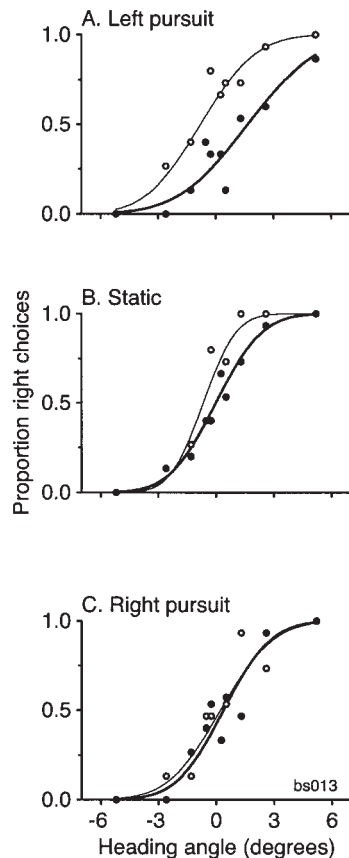
Figure 9. Example of microstimulation in the presence of smooth pursuit. We now separately plot the animal's choices and fit functions for each of the three pursuit conditions. Conventions are as in Figure 7. The neurons at this site preferred left headings.

Figure 10. Schematic illustrating different microstimulation effects. In all panels, the dashed line illustrates the control, unstimulated psychometric function, and the solid line illustrates the function with microstimulation. (*A*) A single experiment with an effect only on bias, which was an increase in left choices. (*B*) A case where microstimulation had no effect on bias, but did have an effect on sensitivity. (*C*) A case with effects on both bias and sensitivity. (*D*) Interaction of induced bias effects with pursuit. The magnitude of the function shift is different for the different pursuit conditions, but the sensitivity is unaffected throughout. (*E*) Interaction of induced sensitivity effects with pursuit. In this case, the effect of microstimulation is on the sensitivity to heading (as in *B*) and this sensitivity effect varies with pursuit.

severely diminished under right pursuit (much lower slope, thus higher σ). In all examples in Figure 10*E*, there is no effect on bias. Interactions, however, can occur simultaneously for both bias and sensitivity, and could be either of the sign shown or the opposite.

To explore the prevalence of both main effects and of interactions, we used a hierarchical series of tests – nested analysis (Hoel *et al.*, 1971). The six sets of psychometric data resulting from each experiment were modeled with probit functions with progressively increasing numbers of free parameters. In the most limited case, a single mean and sigma were used to describe all the data. Then, systematic effects of microstimulation were assessed by fitting the stimulation and control data with different means (to detect changes in bias), different values of σ (to detect changes in threshold), or both. Lastly, interactions were tested by including cross terms between pursuit and microstimulation in the model. To test the statistical significance of the terms in the model, we employed likelihood ratio testing. This approach compares the value of two models using the difference of their log-likelihoods. This difference, which is distributed approximately as chi-square, is well behaved. Adding free parameters to a model will always improve the fit and the actual improvement can be compared against the value expected under the null hypothesis that the data are really not different in a way captured by the added parameter. As progressively more relaxed models incorporating more free parameters are fit to the data, the improvement required to achieve significance rises as well. This effectively
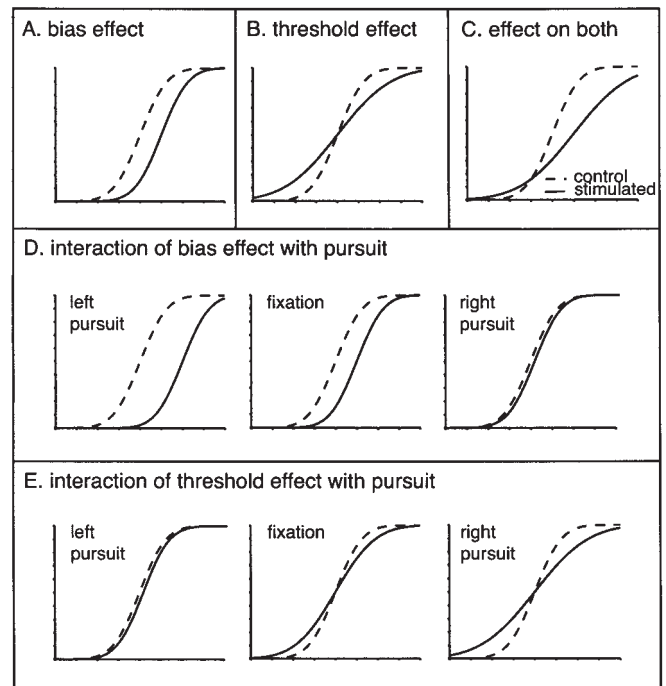
'penalizes' models with too many free parameters, because the expected increase in fit quality grows – even if just fitting noisy data otherwise well described under the null hypothesis.

We used this approach to test all possible effects of microstimulation (Fig. 10). We tested for changes in bias and in threshold, and for the interaction of each of these effects with pursuit conditions. The principle of this hierarchical approach is very similar to that used in stepwise regression; the main difference is that we used a likelihood ratio test to evaluate the significance of each parameter in the model, instead of an *F* ratio. When fitting data that included pursuit, we always incorporated free parameters for pursuit alone; these account for the variable effects that pursuit often had on performance, with or without microstimulation.

The results of this analysis for the entire sample of microstimulation sites (Table 1) indicate that significant effects of microstimulation were frequent, occurring in 60% of the experiments. When significant effects were observed, these nearly always resulted in a significant shift of the function, or a change in bias. Effects of microstimulation on the sensitivity to heading (slope) were less frequent and only very rarely occurred in isolation, without bias effects. A similar pattern emerged from the analysis of pursuit interactions. Such interactions were frequent, occurring in over half of the sample. Again, effects on bias were more frequent than were effects on slope, consistent with the fact that pursuit itself had a larger effect on bias than on sensitivity (Figs 3 and 6).

This analysis described the frequency of significant effects,

Table 1
Frequencies of significant effects of microstimulation on heading psychophysics

	Main stimulation effects				Pursuit interactions			
	Any	Mean	Slope	Both	Any	Mean	Slope	Both
Cases with pursuit (51)	36 (71%)	32 (63%)	19 (37%)	13 (25%)	29 (57%)	29 (57%)	13 (25%)	10 (20%)
Cases w/o pursuit (16)	4 (25%)	4 (25%)	2 (13%)	2 (13%)	–	–	–	–
All cases (67)	40 (60%)	36 (54%)	21 (31%)	15 (22%)	–	–	–	–

Experiments with pursuit included substantially more trials, raising sensitivity to small effects of microstimulation.

but we were equally interested in their magnitudes. These were captured by a shift metric similar to that used above in analyzing the psychophysics. This shift was derived from the multiple fitting procedure described above. The distribution of the magnitude of this principal effect of microstimulation is shown in Figure 11*A*. As in Figure 8 (which analyzed the static trials only), the units of the *x*-axis are expressed relative to the preferred direction of the stimulation site. Positive values correspond to cases where the shift in bias was in the direction predicted by the site's tuning, whereas negative shifts are oppositely directed effects. This distribution has a mean of 0.53, significantly shifted to the right of zero ($t = 2.36$, $P < 0.05$). This average change in bias, across all pursuit conditions, was the baseline effect upon which any additional interactions were superimposed. Note that the magnitude of this shift is somewhat larger – and statistically more reliable – than the average shift on trials without pursuit. This suggests that the bias induced by microstimulation is potentiated by the presence of smooth pursuit.

The modest changes in threshold found without smooth pursuit were also more apparent when pursuit trials were included in the analysis. Figure 11*B* shows the effect of microstimulation on slopes of the psychometric functions, relative to baseline slope observed in the control condition on each experiment. Positive values on this axis correspond to flatter psychometric functions, with higher thresholds. There was a modest but statistically very reliable effect on the slope, averaging 16% ($t = 5.55$, $P < 0.001$).

We next examined whether the tuning of the neurons at the stimulation site predicted the effects of stimulation. To quantify heading tuning, we derived a contrast index comparing the average response across all left headings to the average response across all right headings:

$$\text{heading turning index} = \frac{\text{right response} - \text{left response}}{\text{right response} + \text{left response}} \quad (3)$$

This index is bounded in a range from –1.0 to 1.0; the former indicates strong left heading tuning, whereas the latter indicates equally strong right heading tuning. Values near zero imply no tuning. This tuning index was significantly related ($r = -0.25$, $P < 0.05$) to the bias induced by microstimulation, captured by the average shift of the psychometric function under microstimulation (Fig. 12). Recall that the shift of the function is to the left if right choices are increased and to the left if right choices are increased. Therefore, the negative slope indicates that the relationship agrees with intuition – biases tended to be stronger in a given direction when the neurons at the stimulation site were more strongly tuned in the same direction. Furthermore, this plot shows that effects that were opposite to the tuning were observed when we stimulated sites where the tuning was relatively weak.

Finally, we turn to the question of interaction between pursuit and the effects of MST microstimulation. Statistically significant
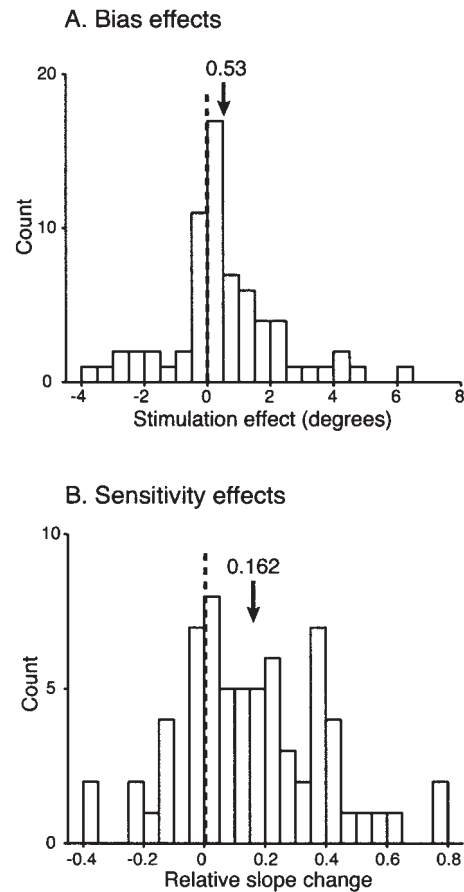

A. Bias effects

B. Sensitivity effects

Figure 11. Summary of microstimulation effects including all trials. We plot changes in bias (*A*) and threshold (*B*) as in Figure 8, but now including all trials. Each single site produced a single main effect of microstimulation, equivalent to the average change of the function across all pursuit conditions. Conventions are as in Figure 8.

interactions were frequent, occurring in about half of the experiments (Table 1). Figure 13 shows the nature of these interactions between induced bias and pursuit condition. For each pursuit condition, we plot the observed stimulation effect (i.e. induced shift) with pursuit against the effect observed when the monkey was fixating (solid symbols, right-tuned sites; open symbols, left-tuned sites). Points off the diagonal represent changes in effect for the site when pursuit was added. The marginal histograms show the frequency distributions of effect magnitude for each condition. Several results are evident in this figure. First, the slopes of the clouds of points are greater than unity; this indicates that stimulation effect magnitude is greater with pursuit than without. Second, the clouds of points are offset above the diagonal for left pursuit and below it for right pursuit. This indicates that pursuit in a particular direction facilitates the
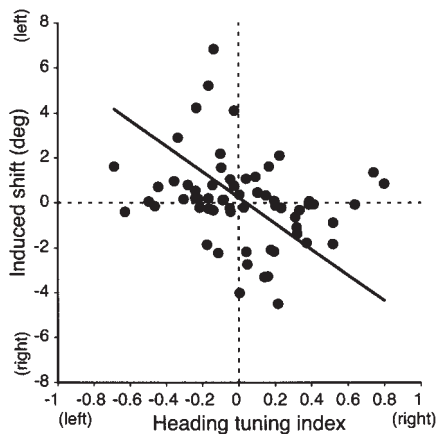
Figure 12. The relationship between site tuning and magnitude of stimulation effect. The heading tuning index is a contrast index expressing the difference between the average responses to left and right headings. The solid line shows the results of linear regression analysis. This indicates that stimulation of more selective sites usually produced bigger perceptual effects. The correlation was significant with either parametric or non-parametric testing. Four cells were omitted from this analysis because quantitative tuning data were not obtained.

Figure 13. The interaction between smooth pursuit condition and the effects of MST microstimulation. In each panel, we plot the effect without pursuit (*x*-axis) against the effect in the same experiment on the interleaved trials with pursuit. Solid symbols denote experiments performed in right-tuned sites; open symbols show those with left-tuned sites. The dashed line indicates equal effect under both conditions. The correlation coefficients under both conditions were significant (left pursuit, 0.75; right pursuit, 0.71) and the slopes in both relationships were significantly greater than one (regression assuming equal variance on *x* and *y*: left pursuit, 2.55; right pursuit, 1.45).

effect of microstimulation in the same direction, independent of the magnitude of the effect without pursuit. The combined effect of both of these changes is to spread out the distribution of effects in the marginal histograms along the right side and, especially, to separate the right-tuned and left-tuned effects from each other. However, there is still considerable overlap even with the pursuit included. Overall, we conclude that stimulation has stronger and more consistent effects during smooth pursuit than without it.

Discussion

In this paper we have demonstrated that selective activation of heading-selective regions within area MST can produce substantial effects on the perceived direction of self-motion when this is simulated visually. Thus, MST signals directly influence decisions on a heading discrimination task. Effects of microstimulation were heterogeneous in sign and magnitude and interacted with the presence of ongoing smooth pursuit eye movements in many cases. This suggests that MST signals are important in the process of correcting heading perception for optic flow field distortions produced by eye movements.

Technical Issues

The first important question to consider is the task itself. It is important to the interpretation of these results to consider whether the monkeys were perceiving the global pattern of motion, or simply performing a linear (even local) direction or speed discrimination. In a complex, cue-rich stimulus such as ours, it is difficult to know unequivocally what cue was being used. However, the overall similarity of the monkey psychophysics with published human psychophysical work provides one strong indication. Human observers trained on heading tasks attempt to use global cues rather than local ones; this maximizes performance. If our monkeys were using local cues instead, their performance would probably have been much worse. In addition, local cues change substantially and systematically with heading eccentricity and with pursuit, yet our monkeys showed little systematic effect of these manipulations on their performance. Therefore, we believe it likely that our monkeys and human observers use similar global cues. Of
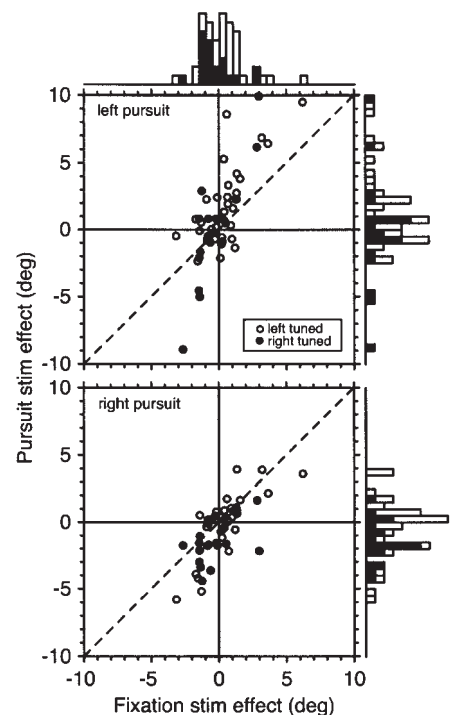
course, the cues in use are impossible to know for certain, especially in nonhuman primates.

Microstimulation is an artificial perturbation of the complex local circuits of the cortex and it is important to think carefully about potential pitfalls in interpretation. The most obvious concern is the extent of current spread, which we cannot directly measure. Based on similar experiments in the better-understood architecture in MT, Newsome and colleagues (Salzman *et al.*, 1992; Murasugi *et al.*, 1993) have estimated that currents such as ours should spread ~150 µm from the electrode tip. This is also consistent with 2-deoxyglucose labeling measurements made in the smooth cortex of the owl monkey (Tootell and Born, 1991) and with dual electrode experiments in motor cortex (Asanuma, 1981). This dimension is below the typical dimensions of clusters of similarly tuned neurons in MST (Britten, 1998), suggesting that direct current spread is largely within a column. We were also concerned about whether current would spread to underlying white matter and that this might produce unpredictable effects. To address this, we performed a small number of experiments with the electrode intentionally lowered into the white matter underlying MST, ~250 µm from the exit from grey matter. In none of these four experiments were any effects of microstimulation observed. Therefore, the effects reported here are likely due to the direct activation of the local circuit surrounding the electrode.

Another concern for the experiments involving pursuit is whether microstimulation influenced the pattern of eye movements, which might spuriously introduce interactions. Indeed, Komatsu and Wurtz showed pursuit gain changes after stimulat-

ing MST, but their stimulation currents were much larger than ours (Komatsu and Wurtz, 1989). Nonetheless, to test this possibility, we measured eye movements in a subset of four experiments in which significant microstimulation effects were seen. We removed saccades from eye-movement records using a velocity criterion, and compared eye velocities on stimulation trials to those on control trials. In no case did we see the slightest trend toward a change in velocity during microstimulation. This analysis was sufficiently sensitive that 1% changes in pursuit gain would have been detected. Therefore, we believe that direct effects of microstimulation on eye movements did not substantially influence our results.

Heterogeneity of Results

Approximately a third of our experiments revealed effects of microstimulation opposite to those that were expected based on the preferences of neurons at the stimulation site. Although such a pattern of results is still consistent with MST signals being used in the judgement of heading, interpretation becomes more difficult. Such mixed results were almost never seen by Celebrini and Newsome in their microstimulation experiment exploring a discrimination between opposite directions of uniform, linear motion (Celebrini and Newsome, 1994b). Several possibilities remain open to explain this apparent difference.

One possible explanation lies in the task – ours is a 'just noticeable difference' task, where the alternatives are much closer to each other along the relevant stimulus dimension. This task design should, in principle, change the 'readout' from MST, perhaps making the results of microstimulation less predictable from neuronal preferences.

Another, more likely possibility lies in the nature of the architecture in MST. Tuning for complex optic flow patterns is not as common in MST as tuning for direction of linear motion (Duffy and Wurtz, 1991). Our data are consistent with this: most of the sites that reached criterion length preferred linear motion with a horizontal flow component (making them tuned for extreme headings). Therefore, the local heterogeneity of single cell signals might be greater along the dimension of heading than along the dimension of linear motion direction. This in turn could cause the net effect of stimulating a column to be less predictable from the multiunit measurements of tuning. This possibility is supported by the relationship shown in Figure 13. The more weakly tuned the site, the more likely we were to get a 'backward' result. This could result either from activation of a subset of signals within the column being activated, or because activation of regions outside the column overwhelmed the within-column effects. At the very least, better neuronal tuning to linear motion might alone have produced the more consistent results in earlier experiments (Celebrini and Newsome, 1994b).

Lastly, it is likely that some columns of MST neurons are involved in other perceptual roles besides heading. For example, the percept of structure from motion involves many of the same signals as does heading; both require the extraction of three-dimensional depth structure from the optic flow pattern. If, for example, a column of neurons more affiliated with structure-from-motion were activated, the resulting percept might have led to unpredictable reports in our heading task. The possibilities we have discussed are not exclusive; many factors may contribute to the heterogeneity of our results.

The Role of MST in Heading Perception

These experiments have provided positive evidence for the use of MST signals in heading tasks and in the compensation of performance on such tasks for the effects of eye movements. The sign of the interaction effects in our experiments was such that, on average, the effect of microstimulation produced larger biases in the direction of the pursuit movement. This is the sign of bias expected if eye movements were incompletely compensated, as retinal image flow opposite the pursuit direction would indicate headings to that side. From the psychophysical measurements, we have seen that monkeys are able to compensate for pursuit and one of ours even overcompensated. The finding that activation of MST signals led to less compensation for pursuit suggests that MST signals are signaling the direction of retinal image flow, rather than being transformed into head- or body-centered coordinates. This is consistent with results from Andersen and colleagues (Bradley *et al*., 1996; Shenoy *et al*., 1999), which indicate that compensation of MST tuning for ongoing head or eye movements is incomplete.

The effects of microstimulation were larger and more consistent under pursuit than when the monkey was merely fixating. This suggests that the representation in MST is more engaged in heading perception when the animal is actively compensating for ongoing eye movements. MST contains extraretinal signals of pursuit eye movements (Newsome *et al*., 1988) and the tuning of MST cells is at least partially compensated for the distortions produced by such movements (Bradley *et al*., 1996; Shenoy *et al*., 1999). Therefore, if heading perception is guided by signals in multiple areas, for instance both MT and MST, the signals in MST might be more influential while pursuit is underway. In turn, this suggests fairly sophisticated gating of the outputs of such high-order sensory areas. Evidence for such gating has recently been uncovered in area MT (Seidemann *et al*., 1998). In general, this notion is consistent with the idea that 'vision for action' is an important function of the dorsal extrastriate area (Goodale, 1998). Although the strongest versions of this hypothesis are clearly challenged by the substantial body of work connecting signals in dorsal extrastriate areas to perception, hybrid versions of the idea are attractive.

Although this work strongly supports the use of MST in heading tasks, microstimulation experiments do not provide much information as to the mechanism of heading perception. The results of the present experiment are consistent with a variety of models relating MST physiology to perception and more traditional methods of quantitative physiology will be required to understand further the cortical mechanisms of self-motion perception.

Notes

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