Published as: *J Neurophysiol.* 2000 October ; 84(4): 1748–1762.

Context-Dependent Smooth Eye Movements Evoked by Stationary Visual Stimuli in Trained Monkeys

Masaki Tanaka^{1,2} and Stephen G. Lisberger¹

¹Howard Hughes Medical Institute, Department of Physiology and W. M. Keck Foundation Center for Integrative Neuroscience, University of California, San Francisco, California 94143

²Department of Physiology, Hokkaido University School of Medicine, Sapporo 060, Japan

Abstract

The appearance of a stationary but irrelevant cue triggers a smooth eye movement away from the position of the cue in monkeys that have been trained extensively to smoothly track the motion of moving targets while not making saccades to the stationary cue. We have analyzed the parameters that regulate the size of the cue-evoked smooth eye movement and examined whether presentation of the cue changes the initiation of pursuit for subsequent steps of target velocity. Cues evoked smooth eye movements in blocks of target motions that required smooth pursuit to moving targets, but evoked much smaller smooth eye movements in blocks that required saccades to stationary targets. The direction of the cue-evoked eye movement was always opposite to the position of the cue and did not depend on whether subsequent target motion was toward or away from the position of fixation. The latency of the cue-evoked smooth eye movement was near 100 ms and was slightly longer than the latency of pursuit for target motion away from the position of fixation. The size of the cue-evoked smooth eye movement was as large as 10°/s and decreased as functions of the eccentricity of the cue and the illumination of the experimental room. To study the initiation of pursuit in the wake of the cues, we used bilateral cues at equal eccentricities to the right and left of the position of fixation. These evoked smaller eye velocities that were consistent with vector averaging of the responses to each cue. In the wake of bilateral cues, the initiation of pursuit was enhanced for target motion away from the position of fixation, but not for target motion toward the position of fixation. We suggest that the cue-evoked smooth eye movement is related to a previously postulated on-line gain control for pursuit, and that it is a side-effect of sudden activation of the gain-controlling element.

INTRODUCTION

When a small moving target appears in the peripheral visual field, primates use two classes of voluntary eye movements to stabilize the target images on the fovea. Smooth pursuit is a continuous eye movement that reduces the velocity of the target images, whereas saccades are rapid, transient eye movements that bring target images onto the fovea. Although combinations of saccadic and smooth pursuit eye movements are used to track a moving object in daily life, these eye movement systems have been examined separately, leading to the general rule that position errors and stationary stimuli cause saccades while moving targets are generally required to evoke smooth pursuit.

In a classical experiment, Rashbass (1961) showed that smooth motion is the main source of visual drive for pursuit initiation. When a step-ramp target motion is configured with steps and

ramps in opposite directions, pursuit is initiated away from target position but in the direction of target motion. In spite of the general consensus that visual motion provides the main sensory drive for pursuit, a variety of papers have also analyzed the effect of target displacement on smooth eye velocity, and some have demonstrated clear effects (e.g., Carl and Gellman 1987; Morris and Lisberger 1987; Wyatt et al. 1989). The most recent suggestion of a possible effect of target position on pursuit has come from the finding that electrical stimulation of the fixation zone of the superior colliculus alters the initiation of pursuit (Basso et al. 1997). Thus there is a clear precedent for pursuit to be affected by visual inputs from stationary targets.

All the experiments mentioned above reported pursuit *toward* the real, or electrically stimulated, retinal position error. A recent study has demonstrated that monkeys can also generate smooth eye movements *away from* the position of a stationary visual stimulus, called a “cue,” if the experimental conditions are contrived properly (Tanaka and Fukushima 1997). The goal of the present study was to define the requisite stimulus conditions for the cue-evoked smooth eye movement more fully and to try to relate it to properties of pursuit that have been identified in previous studies. We will conclude that the cue-evoked eye movement may be related to a pursuit gain control element that has been suggested in previous experiments as a way to explain a number of observations (e.g., Grasse and Lisberger 1992; Schwartz and Lisberger 1994). We devote the remainder of the INTRODUCTION to a consideration of the evidence regarding the existence and nature of the on-line gain control.

The best evidence for a pursuit gain control comes from experiments showing that the smooth eye velocity evoked by a given brief perturbation of target motion depends on the initial conditions. The size of the response depends on eye/target speed at the time of the perturbation: the response is small but present if the perturbation is delivered during fixation or during the offset of pursuit and large if the perturbation is delivered during the maintenance of pursuit at target speeds in excess of 20°/s or during the onset of pursuit (Goldreich et al. 1992; Krauzlis and Miles 1996a; Schwartz and Lisberger 1994). The presence of on-line gain control was interpreted as evidence that continuous variation in the gain of visuomotor processing was a component of the neural mechanisms controlling pursuit. As originally suggested by Robinson (1965), the gain would be very low and the pursuit system rendered “off” during fixation of a stationary target and the gain would increase to a varying degree to render the pursuit system “on” after the decision to track a moving target.

In another relevant paper, Lisberger (1998) demonstrated that pursuit was automatically enhanced in the immediate wake of a saccade. Further, even though presaccadic pursuit depended strongly on the position of the moving target (see also Lisberger and Westbrook 1985), enhancement was spatially uniform and caused postsaccadic eye velocity to be independent of the position of the pursuit target before the saccade. Lisberger’s (1998) interpretation was that saccades could increase the gain of pursuit and automatically render the pursuit system “on.” In contrast, the status of the gain control before the saccade depended on the exact configuration of the step-ramp target motion. If the ramp took the target away from the position of fixation, then the gain remained low and pursuit was weak. If the ramp was going to bring the target onto the fovea soon, then the gain was increased and presaccadic pursuit was excellent. Thus he proposed that the toward/away asymmetry in pursuit resulted from a toward/away asymmetry in activation of the pursuit gain control element. We will show a striking parallel between the proposed toward/away asymmetry in the gain control and the directional bias reflected in the cue-evoked eye movements analyzed in this paper. Based on this parallel, and the finding that the cue itself can enhance presaccadic pursuit for targets moving away from the position of fixation, we suggest that the cue-evoked smooth eye movements are a manifestation of sudden changes in the value of the pursuit gain control.

METHODS

Animal preparation

Five male monkeys were used in this study. Experiments with three rhesus monkeys (*Macaca mulatta*, monkeys *KLB*, *NNK*, and *PCK*) were conducted at the Department of Physiology, University of California, San Francisco. Experiments with two Japanese monkeys (*Macaca fuscata*, monkeys *SSK* and *KRS*) were conducted at the Department of Physiology, Hokkaido University School of Medicine, Sapporo, Japan. All experimental protocols described below were approved in advance by the Institutional Animal Care and Use Committee at the respective universities.

The experimental procedures for the rhesus monkeys were similar to those described previously (Lisberger and Westbrook 1985). After initial behavioral training, the animals were sedated with ketamine hydrochloride and anesthetized with isoflurane. Using sterile procedure, a head holder was installed with dental acrylic, and a coil of wire was implanted under the conjunctiva to record eye movements (Fuchs and Robinson 1966; Judge et al. 1980). The surgical methods for the Japanese monkeys have been described elsewhere in detail (Tanaka and Fukushima 1998). Briefly, the animals were anesthetized with pentobarbital sodium and halothane. A pair of head holders and an eye coil were implanted with sterile procedure. All animals were trained to sit in a primate chair. During experiments their heads were restrained by the implanted head holder.

Visual stimulus and behavioral tasks

For experiments done in San Francisco, visual stimuli were presented on a Pentium PC controlled analog oscilloscope (Hewlett Packard 1321B or 1304A) with a refresh rate of 250 Hz. The oscilloscopes were located either 45 or 28 cm away from the eyes and, because they had different sized screens, subtended similar visual angles of $44.4 \times 36.3^\circ$ or $42 \times 36^\circ$. The visual stimuli were 0.2 and 0.6° white square spots with luminances of 3.8 and 17.6 cd/m^2 , respectively. The smaller spot served as both a fixation target and a moving pursuit target. The larger spot was used to provide a salient, stationary stimulus that we refer to as a “cue.” For experiments done in Sapporo, a red laser spot (0.25°) projected onto the back of a translucent tangent screen (55 cm from the eyes) was used as both the fixation target and pursuit target. The target position was controlled by a pair of mirror galvanometers. The mirror position was updated every millisecond by a Macintosh computer. An array of green light-emitting diodes (LEDs) was attached on the screen to provide the visual cues (Fig. 1A). The array consisted of nine LEDs placed just above the horizontal meridian at 0, 5, 10, 15, and 25° right and left of the vertical meridian and two LEDs placed on the vertical meridian 10° above and below the central fixation target. We were unable to measure the luminance of the visual stimuli used in Sapporo. However, we can report that they were configured with the cue much brighter than the target spot, and they were consistent in luminance from day-to-day.

The basic paradigm for target presentation and motion was a modified step-ramp pursuit task (Rashbass 1961). Each trial began with the appearance of a central fixation spot. After a random fixation period (1–1.5 s), the target spot jumped to the right or left and moved smoothly along the horizontal meridian. The monkeys were required to track the moving spot with their eyes to obtain a liquid reward. In many trials, we introduced a temporal “gap” between the offset of the fixation target and the appearance of the moving target, because a previous study showed that eye movement responses to a peripheral visual “cue” are enhanced if the cue appears during such a gap (Tanaka and Fukushima 1997). The fraction of the gap trials in a block ranged from 0 to 100%, but usually was more than 80%. For experiments done in Sapporo, a 20-ms gap was always introduced to avoid any visible streak caused when mirror galvanometers attempted to execute a step of target position.

Different monkeys received different experience with respect to the direction of target motion relative to the position of fixation. For the two Japanese monkeys (*SSK* and *KRS*) the target always moved toward the central fixation target from an eccentric position (“toward” pursuit trials e.g., Fig. 1*B*). For two of the rhesus monkeys (*KLB* and *NNK*), most prior experience was with randomized directions of target motion, so there was approximately equal probability that the target would move toward or away from the position of fixation. Except for one experiment (Fig. 3, *B* and *D*), we retained that design in all blocks of trials for the present experiments: the tracking target moved toward or away from the fixation target with equal probability. The remaining rhesus monkey (*PCK*) had not participated in any experiments prior to these and was trained only with tracking targets that moved away from the fixation target (“away” trials). During the initial pursuit training and data collection, which lasted 6 wk, this monkey never saw target motion toward the position of fixation.

In most trials, a larger square spot (San Francisco) or one of the green LEDs (Sapporo) was presented briefly (25–300 ms, usually 100 ms) during the gap period as a visual cue. The location of the visual cue and the direction of target motion were randomized within each experiment so that the monkey could not predict the direction of pursuit by the location of the cue. Figure 1*B* illustrates the experimental paradigm we used. In this example, the gap between the offset of the fixation target and the onset of the tracking target was 200 ms, and the cue was visible for the last 100 ms before the appearance of the tracking target. The cue appeared either 5° to the left or right of the central fixation target. The pursuit target also appeared at 5° right or left, moved at 30°/s for 666–1,000 ms, and then stopped and remained visible for an additional 300–500 ms. Intertrial intervals were 500–1,000 ms. Each block of trials consisted of up to 68 different variations of the temporal and spatial parameters of the basic trial configuration described above. For example, data depicted in the bottom of Fig. 7*B* were obtained from a block of 64 different cued trials (2 pursuit directions × 2 step directions × one gap duration × 8 cue-lead times × 2 cue locations) and 4 no-cue controls (2 pursuit directions × 2 step directions). Data in Fig. 6, *A* and *C*, were obtained from a block of 60 different combinations (2 pursuit directions × 2 step directions × 5 gap durations × 3 cue conditions). In one experiment, we presented the visual cue during gap saccade trials (Fig. 3, *A* and *C*). The monkeys were rewarded with water or juice when they kept their eye position within 2–5° of the moving target for the duration of the trial. In the initial phase of training for those experiments, monkeys frequently made saccades to the visual cue, especially in trials with a gap. As training progressed, monkeys gradually learned to suppress saccades to the cue, so they could track the moving target adequately. We usually mixed many combinations of trials with different cue location, lead-time, and gap duration to train monkeys to learn not to respond to the cue. Data were collected only after the monkeys were well trained in the cue paradigm. Experiments were carried out in a dark room, except for a subset described in the text or illustrated in Fig. 11. For the experiments with some ambient illumination, we estimated the ambient illumination by covering the dark face of the display oscilloscope with white paper and using a photometer to measure the luminance of the paper from the position of the monkeys’ eyes. The ambient luminance level measured in this way was 0.51 cd/m².

Data acquisition and analysis

Horizontal and vertical eye velocity signals were obtained by analog differentiation (band-pass DC to 25 Hz, –6 dB/oct or DC to 50 Hz, –12 dB/oct). Data were digitized and sampled at either 1 kHz (San Francisco) or 500 Hz (Sapporo). Eye movements were analyzed by using homemade interactive computer programs. We first reviewed both eye position and velocity traces from each trial on the video monitor. The programs allowed us to visually detect the onset and the offset of each saccade and mark them with a mouse-controlled cursor. These saccadic portions of the eye velocity traces were not used in subsequent analyses. Unusually noisy trials or trials in which the monkey clearly did not attempt to track the moving target or

made a reflexive saccade to the visual cue were eliminated from analyses. Horizontal eye velocity traces were aligned on the onset of target motion for identical tasks in the same block. We then made averages of eye velocity as a function of time, or measured eye acceleration and velocity at selected times in individual trials as described below. Because the magnitude of eye movement responses varied from day to day, data were compared only within single experimental days.

Quantitative analysis entailed measurement of eye velocity immediately before, and eye acceleration during, the initiation of pursuit. In most of our experiments, the cue appeared 100 ms before the onset of target motion, so that the normal onset of pursuit would coincide with the peak of the smooth eye movement evoked by the cue. Therefore we chose the time of the onset of pursuit for step-ramp target motion without a cue as the time for analysis of the response to the cue. Probably because of differences in the exact visual display used at the two sites, the monkeys used in San Francisco had slightly shorter pursuit latency (~100 ms in the “toward” trials, ~80 ms in the “away” trials) than those used in Sapporo (~120 ms in the toward trials). We estimated the size of the response to the cue by measuring eye velocity at the relevant time from individual trials (80 and 100 ms after target motion onset for the San Francisco and Sapporo experiments).

We measured eye acceleration from averages of eye velocity based on more than 15 individual desaccaded traces, by fitting a regression line to the average eye velocity for an 80-ms period starting at the onset of pursuit. The onset of pursuit was detected using a technique similar to the one developed by Carl and Gellman (1987). Briefly, baseline eye velocity was analyzed by computing the mean and standard deviation (SD) of eye velocity for the interval from 100 ms before to 50 ms after the onset of target motion. Then a regression line was fit to the average eye velocity for the period from 10 ms before to 30 ms after the average eye velocity was more than 2 SD above the baseline mean. The point where the regression line intersected the mean baseline eye velocity was taken as the pursuit onset. Because the monkeys often initiated catch-up saccades during this period, we were sometimes unable to obtain average traces for 80 ms when the target moved away from the fixation target. In such cases, eye acceleration was measured from average eye velocity for a period <80 ms.

RESULTS

Figure 2 shows data from three individual trials that delivered the same rightward target motion at 30°/s with a 200-ms gap period between the offset of the fixation target and the onset of the tracking target. The position and velocity traces in Fig. 2 begin at the time when the fixation target disappeared. If we did not present a cue in the gap period (Fig. 2A), then the gap had no apparent effect on pursuit, and rightward eye velocity was initiated with a normal latency of ~100 ms. If a cue appeared during the gap period, 100 ms before the onset of target motion (arrowheads in Fig. 2, B and C), then eye velocity became nonzero during the normal latency of pursuit. When the cue was presented at 5° right (Fig. 2B), there was a substantial leftward deviation in eye velocity, beginning about the time when the tracking target appeared. When the cue was presented at 5° left (Fig. 2C), rightward eye velocity began at about the time the tracking target appeared. In toward pursuit trials like those shown in Fig. 2, catch-up saccades either did not occur during the initiation of pursuit or were delayed until after the first 100 ms of pursuit. Note that with extensive training the monkeys were able to prevent saccades to the visual cue even though its size (San Francisco) or color (Sapporo) made it seem to us more salient stimulus in the display.

Context specificity of the smooth eye movements evoked by a visual cue

The occurrence of the cue-evoked smooth eye movements depended on whether the cues were delivered during blocks of saccade or pursuit trials. In Fig. 3, each point plots horizontal eye

velocity 80 ms after the onset of target motion, and the points are plotted in the order that the trials were delivered. Since trials that presented cues on the left (open symbols) or right (filled symbols), or no cues (solid trace near zero eye velocity) were randomly interleaved, each of these trial types is well represented at each time point. The experiments analyzed in Fig. 3, A and C, consisted of three successive blocks of trials containing 700 pursuit trials, 600 saccade trials, and then 700 more pursuit trials. Pursuit trials were selected randomly from 12 different combinations of the following: two initial positions for the tracking target (right or left of fixation), two directions of target motion (i.e., away or toward the position of fixation), and three cue conditions (right, left, or without a cue). The initial position of the tracking target was always $\pm 5^\circ$, and its velocity was $\pm 30^\circ/\text{s}$. When it was delivered, the cue appeared either 5° right or left of the fixation target for 100 ms before the onset of motion of the tracking target. Saccade trials were delivered with a similar design, except that the tracking target was supplanted by a stationary target that appeared at 10° right or left after the 200-ms gap period and stayed there for 1,000–1,500 ms.

Inspection of Fig. 3, A and C, reveals that the direction of the eye movements measured just before the onset of pursuit was consistently away from the position of the cue, even though there were large intertrial variations in the magnitude of eye velocity. In contrast, moving averages of eye velocity for every 15 consecutive trials without a cue showed essentially zero eye velocity (continuous thick line). The running standard deviation of eye velocity for trials without a cue (not shown in Fig. 3) ranged from 0.28 to $1.87^\circ/\text{s}$ (monkey *KLB*) or from 0.16 to $0.95^\circ/\text{s}$ (monkey *NNK*), indicating that the average eye velocities near zero reflected a consistent absence of a response in the absence of the cue, and not alternation between large leftward and rightward responses. Comparison of the magnitude of the cue-evoked eye velocity during blocks of pursuit and saccade trials shows a large effect on the responses. The cue-evoked smooth eye velocity was much larger in pursuit blocks than in saccade blocks, but was similar in the pursuit blocks that came before and after the saccade blocks. For the data in Fig. 3, A and C, statistical analysis of successive saccade and pursuit blocks revealed significant differences for all four possible comparisons (unpaired *t*-test, $P < 0.001$).

We have not attempted to analyze the time course of the transition quantitatively, but it is clear from Fig. 3, A and C, that it occurs within 100 trials, both at the switch from pursuit to saccade trials and the switch from saccade to pursuit trials. These results suggest that the occurrence of the cue-evoked smooth eye movements is related to the behavioral state of the monkeys, in particular, to the preparation for a target motion that will require smooth pursuit. Note that the direction of the cue-evoked smooth eye velocity is not related to the direction of motion of the tracking target, since rightward and leftward target motion, and toward and away trials, were randomly interleaved in trials that presented cues on the left or right. For example, the open symbols in the first block of Fig. 3A represent measurements made from trials that presented a cue on the left in the temporal gap before leftward or rightward target motion toward or away from the position of fixation. Yet, the cue-evoked eye velocities were all rightward.

Monkeys could change the magnitude of the cue-evoked smooth eye movements within 100 trials. Could they also change the direction of the cue-evoked smooth eye movements if the blend of pursuit trials provided a consistent expectation about target motion? Although the monkeys used in Fig. 3 had received extensive previous experience with an approximate balance of toward and away pursuit trials, it is plausible that they had come to expect target motion toward the fixation target rather than that away from the fixation target. If so, then the monkeys might initiate anticipatory eye movements in the direction opposite to any visual stimulus in the anticipation that the stimulus would shortly move toward the position of fixation. We evaluated this possibility by experiments that delivered blocks of away and toward trials separately, where trials included the same 200-ms gap between the offset of the fixation target and the appearance of the tracking target. Figure 3, B and D, shows data from two such

blocks of pursuit trials. In the first block, the pursuit target always moved in the same direction as the preceding target step (i.e., away pursuit trials). The first three hundred trials in the away block did not present a visual cue, and the subsequent 500 trials had an equal probability of no cue, a left cue, or a right cue. This was followed by a similar block of 800 toward trials, again with cues absent from the first 300 trials. Figure 3, *B* and *D*, shows that the direction of the cue-evoked smooth eye velocity was not altered when all trials took the tracking target away from the position of fixation. This contrasts with the ability of the same monkeys to change the size of the cue-evoked response within 100 trials when the blocks switched from saccade to pursuit trials (Fig. 3, *A* and *C*). The magnitudes of the eye movements away from the cue *decreased* in the toward pursuit trials in one monkey (*KLB*, unpaired *t*-test, $P < 0.01$), possibly because of fatigue. No statistically significant difference in the size of the cue-evoked smooth eye movement was observed in the comparison of away and toward blocks for the other monkey (*NNK*).

We next asked whether training a naïve monkey only on away pursuit trials could result in cue-evoked smooth eye movements *toward* the visual cue. Figure 4*A* shows the time courses of rightward pursuit obtained from *monkey PCK* after his initial 6 wk of behavioral training in which he was exposed only to targets that moved away from the position of fixation. It was a challenge to obtain strong cue-evoked smooth eye movements in monkeys that lacked extensive experience in pursuit tasks, so we chose conditions that would optimize the responses in this monkey. In this example, the duration of the gap between fixation target offset and tracking target onset (vertical dashed line) was 300 ms, and the cue appeared at 5° right for the last 150 ms before the tracking target appeared at 5° right and moved away from the position of fixation. The time of appearance of the cue is shown by the arrowhead. Figure 4*A* shows that this configuration of the gap and cue sometimes evoked tiny eye movements toward the visual cue (rightward in this case) followed by larger smooth eye movements away from the cue. The initiation of rightward pursuit then reversed the cue-evoked smooth eye movement. Since the smooth eye movements away from the cue were observed in trials without the tiny eye movements toward the visual cue (data not shown), the cue-evoked eye movements away from the cue were not due to the retinal slip of a stationary visual cue caused by the tiny eye movements toward the cue observed in this monkey. For comparison, Fig. 4*B* shows data from a different monkey in similar away pursuit trials, in which the cue appeared at 5° right for the last 100 ms of a 200-ms gap. The cue-evoked smooth eye movements had similar latencies of ~100 ms, similar time courses, and both took the eyes away from the position of the cue. Because the cue-evoked smooth eye movements took the eyes smoothly away from the position of cue even in a monkey that had never received training in the toward pursuit paradigm, we conclude that the direction of the cue-evoked smooth eye movements cannot be attributed entirely to past experience on toward pursuit trials.

Table 1 summarizes the average sizes ($\pm$ SD) of the cue-evoked eye velocity examined in this study. The values are averages of the data from two to nine different experiments for each monkey, and the standard deviations indicate variation of the average size across days. These data show that the cue-evoked eye movements in *monkey PCK* were in the same direction as in the other monkeys but were generally of smaller size. Since the magnitude of the eye movements showed large intersubject as well as interexperiment variability, we have not attempted further comparison between the data from different days or monkeys.

Latency and time course of cue-evoked smooth eye movements

The gap/cue/pursuit paradigm we have used thus far reveals the existence of cue-evoked smooth eye movements, but the visual targets that appear after the cue prevent analysis of the full time course and amplitude of the cue-evoked eye movements. To address this issue, we conducted experiments in which most of the trials consisted of the same blend of trials used in

the pursuit blocks in Fig. 3, *A* and *C*, but 10% of the trials served as probes and presented cues without any subsequent visual stimuli. Figure 4, *C* and *D*, shows examples of individual (fine traces) and average (bold traces) eye velocity for two monkeys in probe trials that delivered a 100-ms duration cue at 5° left, starting 100 ms after the offset of the fixation target, followed by a 950-ms gap that terminated at the end of the trial. In both monkeys, rightward smooth eye movements were initiated ~100 ms after the cue onset. Eye velocity peaked 80–110 ms later, and the full response lasted ~250 ms.

Figure 5 compares the latency of the cue-evoked smooth eye movements with the latency for the initiation of pursuit toward or away from the position of fixation in two monkeys. The data plotted in Fig. 5, *A–D*, were obtained from right and left pursuit trials without a cue, and those in *E* and *F* were from rightward toward pursuit trials with right or left cue. Because of the difficulty of measuring the latency of a small smooth eye velocity response reliably, we have adopted a somewhat different approach. For each target motion, we have made averages of eye velocity triggered on the onset of the cue (Fig. 5, *E* and *F*) or the onset of target motion (Fig. 5, *A–D*) and defined the latency of the response as the time when the responses to leftward and rightward stimuli diverged. This revealed a progression from the shortest latency for target motion away from the position of fixation (Fig. 5, *A* and *B*), longer latencies for target motion toward the position of fixation (Fig. 5, *C* and *D*), and the longest latencies by a tiny amount for the cue-evoked smooth eye movements (Fig. 5, *E* and *F*). To make these effects more visible, we have drawn vertical dashed lines at the time of the initiation of pursuit for target motion away from the position of fixation for each of the monkeys (75 ms for *monkey KLB*, 90 ms for *monkey NNK*). We realize that averages of eye velocity give a better indication of the shortest latency response rather than of the average latency. To illustrate that this potential problem was obviated by the consistency of the latencies within each stimulus condition, we have superimposed on the averages (bold traces) all the individual responses for stimuli that evoked rightward smooth eye velocity (fine traces). For *monkey KLB* (*left column*), these individual traces support the progression of latencies from shortest in away trials to longest in cue-evoked eye movements. For *monkey NNK* (*right column*), the individual traces endorse the longer latency of the cue-evoked smooth eye movement, but raise questions about whether the difference in latency between toward and away trials is large enough to be functionally or statistically significant.

Factors that affect the magnitude of the cue-evoked smooth eye movements

GAP DURATION—The magnitude of the cue-evoked smooth eye movements depended on the duration of the gap between the offset of the fixation target and the appearance of the tracking target. For the experiments summarized in Fig. 6, we used gap intervals that varied randomly from 0 to 400 ms in 100-ms increments and, again, measured eye velocity immediately before pursuit initiation. As before, the cue appeared at 5° left or right for the last 100 ms before the onset of the tracking target. In each monkey presented here, the magnitude of the cue-evoked eye velocity was largest when the gap duration was 200 or 300 ms and was smaller when the gap duration was longer or shorter. In all panels in Fig. 6, data obtained from rightward pursuit trials are plotted as open circles and those from leftward pursuit trials as filled triangles. Data for left cue trials are connected by solid lines and those for right cue trials by dashed lines. The average eye velocity in noncue control trials is plotted as symbols without connecting lines. Inspection of Fig. 6 shows that the direction and magnitude of the cue-evoked smooth eye movement depended on the presence and position of the cue (discriminated by solid vs. dashed lines), but not on the direction of subsequent target motion (discriminated by filled vs. open symbols). For *monkey KLB* (Fig. 6, *A* and *C*), studied in San Francisco, essentially the same effects are present for the away and the toward pursuit trials, which have been plotted separately even though they were randomly interleaved during the experiments.

Monkeys KRS (Fig. 6B) and *SSK* (Fig. 6D) were both studied in Sapporo, under conditions in which the tracking target always moved toward the position of fixation.

CUE TIMING—The response evoked by a given cue depended critically on when the cue was presented relative to the offset of the fixation target. The traces in Fig. 7A show averages of eye velocity for rightward pursuit in trials that had different times of cue appearance (triangles) but the same 200-ms gap between the offset of the fixation target (1st vertical dashed line) and the onset of the tracking target (2nd vertical dashed line). Data were aligned on the target motion onset (*time 0*) and averaged separately for each value of cue-lead time. The cue appeared 5° to the right (*top set of traces*) or left (*bottom set of traces*) of the fixation target. If the cue appeared before the moving target (positive values of cue-lead time), then it was extinguished when the moving target appeared. If the cue appeared at or after the moving target appeared (zero or negative values of cue-lead time), then it persisted for only 50 ms. The example traces show an experiment where the cues evoked smooth eye movements ~120 ms after the cue onset, and the amplitude of the responses was largest if the cue appeared during the gap period (between the 2 vertical dashed lines). In this example, the cue evoked little or no smooth eye movement when it appeared before the gap. It was not possible to separate the cue-evoked eye movement from the initiation of smooth pursuit if the cue appeared just before, near, or after the onset of tracking target motion. The magnitude of the cue-evoked eye movement is quantified in the three graphs of Fig. 7B, which plot average eye velocity 200 ms (*monkeys SSK* and *KRS*) or 180 ms (*monkey KLB*) after the onset of the cue as a function of the cue-lead time. We plot eye velocity only for the trials in which the cue appeared 100–300 ms prior to the onset of the tracking target. In two of the three monkeys (*SSK* and *KRS*), the cue caused only a slight smooth eye movement if it appeared while the fixation spot was still present (cue-lead time >200 ms). In the third monkey (*KLB*), the cue was effective even if presented 100 ms before the fixation target was extinguished. We do not have a ready explanation for this variation among monkeys.

CUE LOCATION—Figure 8, A and C, plots averages of horizontal eye velocity immediately before pursuit initiation as a function of the location of the cue in standard trials with a cue-lead time of 100 ms and a 200-ms gap between the offset of the fixation target and the onset of target motion. Cues could appear up to 25° eccentric on the horizontal axis or at 5 or 10° vertical. Trials with different cue locations were interleaved randomly. As before, the tracking target always appeared 5° right or left and moved toward (A) or away from (C) the fixation target at 30°/s. The cue-evoked smooth eye movements were not present when the cue appeared at the position of fixation. They were largest when the cue appeared 5° eccentric along the horizontal axis. They decreased as a function of eccentricity but were still observable when the cue appeared 15° eccentric. Statistical comparison of the size of the cue-evoked smooth eye movements for cues at 0 versus 15° revealed statistically significant differences in all four cases (unpaired *t*-test, $P < 0.001$). No smooth eye movements were observed when the cue appeared above or below the fixation target or did not appear at all (symbols at right of graph, not connected to other points). The cue-evoked smooth eye movements were the same for trials that presented rightward target motion (open circles) and leftward target motion (filled triangles). Data from two other monkeys were nearly identical and are not shown.

TARGET VELOCITY—Since the large cue-evoked smooth eye movements were observed only if the cue was presented in blocks of pursuit trials (Fig. 3, A and C), it is plausible that the size of the cue-evoked smooth eye movement might be related to the speed of target that monkey is preparing to pursue. We therefore asked whether the magnitude of the cue-evoked responses would change in relation to target velocity if individual velocities were blocked so that the target velocity was known ahead of time. We used four (*monkey SSK*) or eight (*monkey KRS*) blocks of trials that consisted of a 200-ms gap, a 100-ms cue-lead time, and subsequent

horizontal target motion at one of 10, 20, 30, or 40°/s. The initial position of the tracking target was 2, 3, 5, and 6° for 10, 20, 30, and 40°/s target motion, respectively. As before, cues could appear with equal probability to the left or right of the fixation position or not at all, and the order of these trials was randomized within each block. Figure 8, *B* and *D*, plot average eye velocity immediately before pursuit onset. The number of trials for each target velocity ranged from 262 to 326 in *monkey KRS*, and from 229 to 236 in *monkey SSK*. Target velocity had a slight but statistically significant effect on the size of the cue-evoked smooth eye movements. Regression slopes were 0.064 and -0.046 in *B* and 0.11 and -0.12 in *D* and were statistically different from zero ($P < 0.05$ for *monkey KRS*, $P < 0.01$ for *monkey SSK*). As before, the direction of the cue-evoked smooth eye movement depended only whether the cue appeared to the right (dashed lines) or left (solid lines) of the fixation target and not on whether the subsequent target motion was rightward (open circles) or leftward (filled triangles).

AMBIENT ILLUMINATION—Significant cue-evoked smooth eye movements were observed only when experiments were carried out in the dark. We compared the magnitudes of the cue-evoked smooth eye movements in alternate blocks of pursuit trials with ambient illumination (0.51 cd/m²), or in the dark for two monkeys. The cue appeared for 100 ms during the 200-ms gap interval either 5° right or left of the fixation target. When the monkeys performed pursuit trials in the dark, the cue-evoked smooth eye movements away from the cue were quite large. For cues presented on the right and the left, they averaged $-4.26 \pm 2.74^\circ/\text{s}$ (mean $\pm$ SD, $n = 228$) and $4.39 \pm 2.39^\circ/\text{s}$ ($n = 218$) in *monkey KLB*, and $-2.77 \pm 2.06^\circ/\text{s}$ ($n = 261$) and $1.60 \pm 1.61^\circ/\text{s}$ ($n = 270$) in *monkey NNK*. The cue-evoked smooth eye movements were still present but were attenuated when the monkey performed same blocks of trials under dimly lighted condition. They averaged $-1.29 \pm 1.66^\circ/\text{s}$ ($n = 204$) and $1.75 \pm 1.96^\circ/\text{s}$ ($n = 180$) in *monkey KLB*, and $-1.11 \pm 0.95^\circ/\text{s}$ ($n = 188$) and $0.38 \pm 0.51^\circ/\text{s}$ ($n = 281$) in *monkey NNK*. The effect of ambient illumination on the velocity of the cue-evoked eye movements was statistically significant for both cue positions in both monkeys (unpaired t -test, $P < 0.0001$).

Enhancement of the initiation of pursuit in the wake of cues

The initial pursuit responses to a step of target velocity have been examined extensively in previous studies (for reviews, see Keller and Heinen 1991; Lisberger et al. 1987). Because the first 100 ms of pursuit initiation is driven by target motion before the eyes begin to move, eye acceleration during the “open-loop” interval is a sensitive measurement to examine visuomotor drive for pursuit. Recent studies have also found that the gain of visuomotor drive for pursuit is subject to on-line gain control (e.g., Schwartz and Lisberger 1994), raising the possibility that eye acceleration in the open-loop interval might be influenced by this on-line gain control. For example, Lisberger (1998) proposed that weak presaccadic pursuit for target motion away from the position of fixation might result primarily from a failure to turn up the gain for visuomotor drive. We now analyze eye velocity during the open-loop interval for target motion toward and away from the position of fixation, to ask whether the cues affect the gain of subsequent pursuit, as well as causing the smooth eye movements we have documented thus far.

Before analyzing the effect of the cue on subsequent pursuit, we developed a cue paradigm that minimized the size of the large cue-evoked smooth eye movements. Figure 9 shows the results of experiments that delivered, with equal probability, no cue, single cues that appeared left or right of the fixation target, or bilateral cues that appeared simultaneously on both sides of the fixation target. As before, each trial had a 200-ms gap between the offset of the fixation target and the appearance of the tracking target. Each graph shows the distribution of eye velocity measured from individual trials just before the normal initiation of pursuit for different cues. Bilateral cues (Fig. 9, *A* and *B*) evoked responses with a narrower distribution of eye velocities than would have been predicted by simply summing the distributions of responses

to right and left cues (Fig. 9, *C* and *D*, filled and open histograms, respectively). However, the responses to bilateral cues remained considerably larger than eye velocity just before the onset of pursuit in trials without a cue (Fig. 9, *E* and *F*).

The wider distribution of eye velocity in the bilateral cue trials than in noncue trials might occur if separate responses to each cue were summed or averaged. To test this possibility, we attempted to predict the distribution of eye velocity in bilateral cue trials based on the data obtained in unilateral cue trials using the following equations

$$\mu = (\mu_1 + \mu_2)/2 \text{ (averaging)} \quad \text{or} \quad \mu = (\mu_1 + \mu_2) \text{ (summation)}$$

$$\sigma = (\sigma_1 + \sigma_2)/2 \text{ (averaging)} \quad \text{or} \quad \sigma = (\sigma_1 + \sigma_2) \text{ (summation)}$$

$$y = [100/\sigma \sqrt{2\pi}] \exp[-(x - \mu)^2/(2\sigma^2)]$$

where μ_1 and σ_1 are the mean and SD of eye velocity for the right cue trials, and μ_2 and σ_2 are those for the left cue trials. The predictions of averaging, plotted as solid curves in Fig. 9, *A* and *B*, were very similar to the data, while the predictions of summation (dashed curves) were too broad. These data are consistent with the possibility that each of bilateral cues evokes smooth eye movements, but that the net smooth eye movement is small because the oppositely directed cue-evoked smooth eye movements were averaged. Of course, it is possible that the distribution for unilateral cues was simply shifted to have a mean value near zero, but we cannot propose any biological or computational mechanism that would produce such a shift.

We next compared the eye acceleration evoked by target motion toward or away from the position of fixation in bilateral cue trials with that in no-cue trials. Because the cue-evoked smooth eye movements were often minimized in the bilateral cue trials, this comparison was not contaminated by the changes in the retinal image motion of the target that would occur if large cue-evoked smooth eye movements preceded the initiation of pursuit. To further improve the validity of this comparison, we selected for analysis only bilateral cue trials in which eye velocity just before the normal onset of pursuit was less than $\pm 1.5^\circ/\text{s}$ (the central 3 bins of the histograms in Fig. 9, *A* and *B*). Figure 10*A* illustrates average eye velocity for trials that provided rightward target motion in the same experiments used to create Fig. 9. These averages were made by eliminating the parts of the traces that corresponded to saccades and then by averaging eye velocity at each millisecond where data from 15 or more trials were available. Because saccades always occurred with relatively short and consistent latencies for target motion away from the position of fixation, this left a gap in the averages where almost all the saccades occurred. Because saccades were infrequent for target motion toward the position of fixation and had highly variable latencies, the traces lack any interruptions.

Figure 10*A* reveals that the presaccadic eye movements of both *monkeys KLB* and *NNK* showed markedly higher eye accelerations in the wake of a bilateral cue (solid traces) than in the absence of a cue (dashed traces), when target motion was away from the position of fixation. In contrast, bilateral cues had relatively little effect on the presaccadic eye velocity for target motion toward the position of fixation. We quantified the changes in initial pursuit response by using the approach described in METHODS to measure presaccadic eye acceleration from traces of average eye velocity. Because of the tendency for early saccades in away trials, analysis of these averages were often based on intervals with durations shorter than 80 ms. In the averages of away trials in Fig. 10*A*, measurements were as follows: *KLB* bilateral cue $192^\circ/\text{s}^2$ over 80 ms; *KLB* no cue, $111^\circ/\text{s}^2$ over 80 ms; *NNK* bilateral cue, $161^\circ/\text{s}^2$ over 42 ms; *NNK* no cue, $51^\circ/\text{s}^2$ over 76 ms.

Figure 10*B* summarizes the effect of bilateral cues on the initiation of pursuit for toward and away trials in all the experiments we conducted on two monkeys. In each graph, the connected

pairs of points compare the responses in bilateral cue trials with noncue trials for a given experimental session, and the left-hand and right-hand stacks of connected points show the responses to target motion away from and toward the position of fixation, respectively. Most of the pairs of points are connected by solid lines, indicating that at least 40 ms of data were available to measure eye acceleration. When delivered in the wake of a bilateral cue, target motion away from the position of fixation evoked responses that were consistently enhanced by comparison with those evoked by the same stimulus in a gap trial without a cue. This difference was statistically significant in each case (paired t -test, $**P < 0.01$, $*P < 0.05$). In contrast, the initiation of pursuit for target motion toward the position of fixation was not consistently affected by the presence or absence of bilateral cues. Note that the enhanced responses to target motion away from the position of fixation in the wake of a bilateral cue remained statistically smaller than the eye acceleration evoked by target motion toward the position of fixation (paired t -test, $P < 0.01$) except for one case (left pursuit of *monkey KLB*, $P = 0.10$).

Since both the initiation of pursuit has shorter latencies and higher eye accelerations when the tracking target appears several hundred milliseconds before its motion onset (Krauzlis and Lisberger 1994a), one might assume that the enhancement of pursuit initiation in away pursuit trials resulted from the fact that one of the bilateral cues appeared at the location where the tracking target started to move. We next asked whether the bilateral cue enhances the pursuit initiation when the initial position of the tracking target is different from the location of either cue. The experiment was carried out in a dimly lit room, and the tracking target started to move from the position of fixation without a gap between fixation target offset and target onset. Figure 11, *A* and *B*, shows the time courses of eye velocity in those trials, and the *inset* of each panel shows the distribution of eye velocity 80 ms after target motion in bilateral cue trials. Again, only the trials with cue-evoked smooth eye velocity less than $\pm 1.5^\circ/\text{s}$ (central 3 bins of each histogram) were included when averaging eye velocity. In both examples illustrated in Fig. 11, *A* and *B*, the initiation of pursuit was enhanced in the wake of a bilateral cue (bold, solid traces), relative to the responses in trials without cues (bold, dashed lines). Relative to the responses to targets moving toward the position of fixation from 5° eccentric (thin, dotted line), the enhanced responses to target motion starting from the position of fixation had arguably lower eye accelerations in this particular experiment.

Figure 11, *C* and *D*, summarizes the data obtained by repeating this experiment four times in *monkey KLB* (*C*) and seven times in *monkey NNK* (*D*). Each trio of connected points compares the initial eye acceleration in trials that presented target motion starting from the position of fixation with or without bilateral cues, and those that presented target motion toward the position of fixation with no cue. For both monkeys (Fig. 11, *C* vs. *D*) and both rightward and leftward target motion (separate graphs in Fig. 11, *C* and *D*), the bilateral cues caused statistically significant enhancement of the initiation of pursuit for target motion starting from the position of fixation (paired t -test, $P < 0.01$). The cue-enhanced eye accelerations evoked by target motion that started from the position of fixation, however, were still smaller than those for target motion toward the position of fixation (paired t -test, $P < 0.01$ for 3 cases, $P < 0.05$ for 1 case).

The bilateral cue paradigms allowed us to examine the effects of the visual cue on the initiation of pursuit by minimizing the cue-evoked smooth eye movements. However, we thought it was also important to attempt analysis of the initiation of pursuit in the wake of single cues, in spite of the fact that these cues also evoked large smooth eye movements. Our strategy was to measure the pursuit response to a given combination of cue and target motion and then subtract the response to the cue alone (cf. Fig. 4, *C* and *D*) from the response to the same cue followed by target motion. The *left columns* of Fig. 12, *A* and *B*, superimpose average eye velocity for target motion with a cue (bold, solid traces), target motion without a cue (dashed traces), and

for a cue without subsequent visual stimuli (fine, solid traces). The *right columns* of Fig. 12, *A* and *B*, superimpose the response to target motion without a cue (dashed trace) and the millisecond-by-millisecond subtraction of the response to the cue only from the response to the cue and the target motion. In the top two conditions for each monkey, which show away trials for *monkey KLB* (Fig. 12*A*) or “non-step” trials for *monkey NNK* (Fig. 12*B*), the “difference” responses to target motion in the presence of a unilateral cue were consistently enhanced relative to the responses to target motion without a cue. As shown earlier in this paper for bilateral cues, the enhancement of pursuit initiation was inconsistent and smaller for target motion toward the position of fixation, and the main effect was a slight change in latency in *monkey KLB*.

Figure 12 used a subtraction analysis to remove the cue-evoked smooth eye velocity before analyzing the response to the onset of target motion, but it failed to correct for the fact that the cue-evoked smooth eye movement also modifies the image motion that ultimately drives the initiation of pursuit. Examples from Fig. 12 show that the apparent enhancement is not due solely to the change in retinal image motion. For the right cues (*2nd row of traces*), the enhanced responses could be attributed to the increase in image motion caused by the leftward cue-evoked smooth eye movement during the initial period of rightward target motion. However, the opposite logic must then apply for left cues (*1st row of traces*); the rightward cue-evoked eye movement should decrease the image motion and decrease the eye acceleration at the initiation of rightward pursuit. Yet, the difference eye velocity responses show enhancement (bold lines in *2nd column of each panel*). We therefore conclude that at least the effect of the cue in the *first row of traces* in Fig. 12, *A* and *B*, reflects enhancement of the initiation of pursuit.

DISCUSSION

Novel form of smooth eye movement

It is accepted widely that visual motion is the main sensory stimulus for the initiation of smooth pursuit. Most studies have found that changes in target position during fixation do not initiate smooth eye movements (Morris and Lisberger 1987; Rashbass 1961). When we altered the standard step-ramp paradigm by incorporating a temporal gap between the offset of the fixation target and the appearance of a moving tracking target, and by training the monkeys to suppress a reflexive saccade toward an extraneous visual “cue” during the gap, smooth eye movements away from the stimulus were consistently evoked by the cue. The cue-evoked eye movements had a latency comparable to or slightly longer than that of normal smooth pursuit (~100 ms). The cue-evoked eye movements were largest when the gap was 200–300 ms, the cue appeared 100–150 ms before the onset of target motion, the cue was 5° eccentric from the position of fixation along the horizontal meridian, and the experimental room was otherwise dark. We think that the use of a new combination of task conditions enabled our discovery of a new form of smooth eye movement that can be evoked without visual motion.

The cue-evoked smooth eye movements reported by Tanaka and Fukushima (1997) and studied in detail here seem to be different from anything reported previously by other authors. Smooth eye movements without visual motion have been reported mostly in human subjects in situations where the direction of subsequent target motion is highly predictable (Becker and Fuchs 1985; Boman and Hotson 1988; Carl and Gellman 1987; Kowler and Steinman 1979). The anticipatory eye movements found in previous studies generally preceded the normal latency of pursuit and consisted of a gradual increase in eye velocity in the direction of predicted target motion. In contrast, the cue-evoked smooth eye movements reported in the present paper were observed when the cue provided no predictable information about the direction of subsequent target motion. In our experiments, the cue-evoked smooth eye movements took the eyes in the wrong direction for half of the subsequent target motions. Although the cue-evoked eye movements were more compelling when the task involved preparation for pursuit eye

movement (Fig. 3, A and C), their appearance during training with “away” target motion in *monkey PCK* makes it impossible to explain their direction purely as trained anticipation that the target would move toward the position of fixation (Fig. 4A). Other studies (Carl and Gellman 1987; Wyatt et al. 1989) have shown that human subjects initiate transient eye movements *toward* the target step in step-ramp pursuit paradigms, in contrast to the cue-evoked eye movements, which take the eyes *away* from the position of a stationary cue. Further, the eye movements evoked in previous step-ramp experiments have been rather small ($\sim 1^\circ/\text{s}$), in contrast to the cue-evoked smooth eye movements reported in the present paper, which often had peak velocity $> 5^\circ/\text{s}$.

The cue-evoked smooth eye movements also do not seem to form the basis for two other features of pursuit that our laboratory has reported previously. 1) Lisberger and Westbrook (1985) reported an asymmetry in the initiation of pursuit that favored target motion toward the position of fixation. We do not think that the asymmetry can be understood as the addition of the cue-evoked eye movement away from the position of the target to otherwise symmetrical initiation of pursuit. The asymmetry of pursuit initiation persisted even when the tracking target appeared eccentric and was stationary for 300 ms before starting to move, an interval long enough for any cue-evoked smooth eye movement to die out. 2) Krauzlis and Lisberger (1994a,b) suggested that three types of visual motion signals contribute to pursuit initiation for a step of target velocity: image velocity, image acceleration, and a motion onset transient. The motion onset transient results from the abrupt onset of image motion and makes a large contribution to the initial ~ 40 ms of pursuit initiation. Two observations make it unlikely that the cue-evoked smooth eye movements are related to the motion onset transient. First, the direction of the cue-evoked smooth eye movements was always away from the cue, whereas the direction of the initial ~ 40 ms of pursuit initiation was the same as target motion and was independent of initial target position (Lisberger and Westbrook 1985). Second, the latency of the cue-evoked smooth eye movements (100–130 ms) was slightly longer than that of the minimal pursuit latency observed in the away pursuit trials (80–90 ms).

Necessary and sufficient stimulus conditions for the cue-evoked smooth eye movement

The presence of a temporal gap between the offset of the fixation spot and the appearance of the tracking target seems to be one necessary condition for large cue-evoked smooth eye movements. The importance of the temporal gap can be appreciated by comparison with the results of experiments published by Krauzlis and Lisberger (1994a) where the tracking target appeared before its motion onset, much as our cues do, but did not evoke a smooth eye movement. The gap that is necessary for expression of the cue-evoked smooth eye movement parallels the necessary conditions for the short latency “express saccades,” which appear when the fixation target is extinguished before the presentation of an eccentric, stationary target. It is known that a temporal gap releases fixation and/or attention systems that are engaged during fixation (Fischer 1987). These systems appear to suppress the initiation of both saccades and pursuit (e.g., Krauzlis and Miles 1996b; Morrow and Lamb 1996), and might also suppress the cue-evoked smooth eye movements during fixation. We suggest that the release of fixation during the gap is necessary for the generation of the cue-evoked smooth eye movement.

Preparation for pursuit eye movements seems to be a second necessary condition for the cue-evoked smooth eye movements. The cue-evoked smooth eye movements were attenuated when the animals initiated saccades to stationary targets in a block of trials. The prior evidence of the difference between neural substrates for saccades and pursuit cause us to favor the idea that the preparation for pursuit is different from the preparation for saccades. Cues might evoke smooth eye movements through neuronal pathways for pursuit that are facilitated when the monkey is preparing for pursuit. It would be possible to develop theories based on a common participation of the collicular fixation zone in small saccades and pursuit eye movements

(Basso et al. 1997; Krauzlis et al. 1997), or smooth eye movements designed to counteract those that might be evoked by the apparent motion at the time of fixation target offset and cue onset. Our data neither support nor refute these possible explanations, and they will not be considered further.

Our data do not reveal whether the presence of a gap and preparation for a pursuit movement are sufficient to enable the cue-evoked smooth eye movement. For example, it may or may not be necessary to provide a cue that looks different from the tracking target. The visual cue used in this study was different in size or color from the moving target, and it appeared at a location selected randomly with respect to the initial position of the moving target. Unfortunately, it was essential to make the cue and tracking target appear different so that the monkeys could be trained not to make a saccade to the cue. In addition, it may prove critical that the stimulus configuration forced monkeys to select the visual stimuli and to make much effort not to respond to the visual cue. We cannot exclude the possibility that our stimulus configuration requires voluntary processes to suppress a reflexive saccade toward the cue, and that these processes in the saccadic and/or fixation systems might be related to the cue-evoked eye movement. It has been shown recently that the saccade motor commands increase the gain of pursuit initiation for a step of target velocity (Lisberger 1998; Ogawa and Fujita 1998; Yang et al. 1999). Perhaps the cue evokes covert saccade commands that are sufficient to activate the pursuit system and cause both the transient smooth eye movements and the enhancement of pursuit initiation for targets moving away from the position of fixation. Given the absence of neural recordings related to the cue, we choose not to speculate further about the neural substrate of the cue-evoked smooth eye movement.

Possible relationship of the cue-evoked smooth eye movement to the pursuit gain control

Several of the recent papers from our laboratory have presented data related to the existence and properties of an on-line gain control for pursuit. The clearest evidence for on-line gain control comes from experiments showing that larger smooth eye movements are evoked by a given brief image motion if the motion occurs during pursuit versus during fixation (Goldreich et al. 1992; Schwartz and Lisberger 1994). A more recent analysis of the postsaccadic enhancement of visuomotor drive for pursuit (Lisberger 1998) has revealed a potential toward/away asymmetry in the gain controller that may be related to the directional bias of the cue-evoked smooth eye movements analyzed in the present paper. We elaborate below.

Analysis of presaccadic pursuit has revealed that the initial eye acceleration depends on the eccentricity of the moving target and on whether it is moving toward or away from the position of fixation (Lisberger and Westbrook 1985). Initial eye acceleration decreases as a function of increases in target eccentricity, and eye acceleration is larger for target motion toward than for target motion away from the position of fixation for targets moving across a given eccentricity. Analysis of postsaccadic eye velocity yields a completely different picture. Neither the initial target position nor the direction of target motion relative to the position of fixation had strong effects on postsaccadic eye velocity (Lisberger 1998; Ogawa and Fujita 1998). Because the eye movements immediately after saccades are driven by visual inputs present before the saccades (Newsome et al. 1985), the lack of a positional or directional bias in postsaccadic eye velocity renders it unlikely that visuomotor drive for pursuit is biased for either target eccentricity or the direction of target motion.

Lisberger (1998) interpreted these data in the context of the pursuit gain control. He suggested that presaccadic pursuit has a toward/away asymmetry and positional dependence because the controller of pursuit gain has these features. The degree of activation of the gain control, and the “gain” of the presaccadic initiation of pursuit would then depend on whether the target was moving toward or away from the position of fixation and on the eccentricity of the moving target. He accounted for the lack of asymmetry or positional dependence of postsaccadic eye

velocity by the suggestion that postsaccadic enhancement was implemented by turning up the pursuit gain control. In accordance with this hypothesis, we propose that the cue used in the present experiments also turns up the pursuit gain control. We suggest that sudden changes in the value of the gain control cause, as a side effect, a command for a blip of eye velocity that is biased by the inherent toward/away asymmetry of the gain controller. In the absence of a fixation or tracking target under conditions of preparation for pursuit, the internal signal causes a cue-evoked blip of eye velocity away from the cue.

Our explanation for the cue-evoked smooth eye movement is supported by the finding that the relationship between its size and the eccentricity of the cue is very similar to the relationship suggested by Lisberger (1998) between the eccentricity of the pursuit target and the degree of presaccadic activation of the gain control. Further, our finding of enhancement of the initiation of pursuit for target motion away from the position of fixation in the wake of bilateral cues is entirely consistent with this interpretation. We suggest that bilateral cues turn up the pursuit gain control, allowing enhancement of the initiation of pursuit while the two cue-evoked smooth eye movements in opposite directions average to a mean response amplitude near zero. The absence of enhancement of the initiation of pursuit for target motion toward the position of fixation would be expected if pursuit gain is already maximal for target motion toward the position of fixation.

Separate control of the pursuit gain and visuomotor drive

Figure 13 shows a conceptual model of pursuit that includes two separate pathways for controlling visuomotor drive and pursuit gain. The basic structure of this model is essentially the same as the ones proposed previously (Grasse and Lisberger 1992; Krauzlis and Lisberger 1994b; Krauzlis and Miles 1996a). In keeping with the suggestions of Lisberger (1998), we assume that visuomotor drive processes its inputs in retinal coordinates, in a way that is independent of target eccentricity. In contrast, the gain of pursuit is controlled by a combination of retinal and extra-retinal signals. To account for the dependence of presaccadic pursuit on target eccentricity, and for the toward/away asymmetries in the responses to both moving targets and stationary cues, we suggest that the inputs to the gain controller are strongly dependent on target eccentricity, favoring stimuli moving toward the fovea. We also suggest that the gain controller receives extra-retinal inputs related at least to saccades, selective attention, and anticipation. We postulate that a sudden increase in pursuit gain cause a small smooth eye movement in the direction of the inherent bias of the gain controller, and that this eye movement is responsible for the cue-evoked smooth eye movements we have recorded in highly trained monkeys.

One curious aspect of the proposal outlined above is the fact that the latency of pursuit is shorter than the latency of the cue-evoked smooth eye movement, at least for target motion away from the position of fixation. If the latter response is a side effect of activating the pursuit gain controller, why does it not have a shorter latency? Perhaps the earliest part of the initiation of pursuit reflects a strong visuomotor drive that is attenuated by the fact that pursuit gain has not yet been increased. This proposal is compatible with the observation that many neurons in the middle temporal area have large transients at the onset of motion (Lisberger and Movshon 1999), since we would expect these transients to drive eye acceleration powerfully if pursuit gain had been increased. It is also compatible with the finding that eye acceleration in the first ~40 ms of pursuit is independent of target eccentricity, while eye acceleration 40–100 ms after the initiation of pursuit assumes the position dependence (Lisberger and Westbrook 1985) that we have tentatively attributed to different levels of the pursuit gain control. We realize that the scenario outlined in Fig. 13 is highly speculative. Yet, it is compatible with available data, and we propose it with the expectation that future physiological experiments will provide critical tests.

Acknowledgements

We are grateful to Drs. K. Fukushima and C.R.S. Kaneko for support and helpful discussion during the earlier part of this study. We also thank H. Rambold, I. Chou, and J. Gardner for valuable comments on the manuscript.

This research was supported by the Howard Hughes Medical Institute, of which S. G. Lisberger is an Investigator and M. Tanaka is an Associate.

REFERENCES

- Basso MA, Krauzlis RJ, Wurtz RH. Microstimulation of the rostral superior colliculus affects pursuit, fixation and saccades. *Soc Neurosci Abstr* 1997;23:844.
- Becker W, Fuchs AF. Prediction in the oculomotor system: smooth pursuit during transient disappearance of a visual target. *Exp Brain Res* 1985;57:562–575. [PubMed: 3979498]
- Boman DK, Hotson JR. Stimulus conditions that enhance anticipatory slow eye movements. *Vision Res* 1988;28:1157–1165. [PubMed: 3257018]
- Burman DD, Bruce CJ. Suppression of task-related saccades by electrical stimulation in the primate's frontal eye field. *J Neurophysiol* 1997;77:2252–2267. [PubMed: 9163356]
- Carl JR, Gellman RS. Human smooth pursuit: stimulus-dependent responses. *J Neurophysiol* 1987;57:1446–1463. [PubMed: 3585475]
- Fischer B. The preparation of visually guided saccades. *Rev Physiol Biochem Pharmacol* 1987;106:1–35. [PubMed: 3112911]
- Fuchs AF, Robinson DA. A method for measuring horizontal and vertical eye movement chronically in the monkey. *J Appl Physiol* 1966;21:1068–1070. [PubMed: 4958032]
- Goldreich D, Krauzlis RJ, Lisberger SG. Effect of changing feedback delay on spontaneous oscillations in smooth pursuit eye movements of monkeys. *J Neurophysiol* 1992;67:625–638. [PubMed: 1578248]
- Grasse KL, Lisberger SG. Analysis of a naturally occurring asymmetry in vertical smooth pursuit eye movements in a monkey. *J Neurophysiol* 1992;67:164–179. [PubMed: 1552317]
- Judge SJ, Richmond BJ, Chu FC. Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res* 1980;20:535–538. [PubMed: 6776685]
- Keller EL, Heinen SJ. Generation of smooth-pursuit eye movements: neuronal mechanisms and pathways. *Neurosci Res* 1991;11:79–107. [PubMed: 1656345]
- Kowler E, Steinman RM. The effect of expectations on slow oculomotor control. I. Periodic target steps. *Vision Res* 1979;19:619–632. [PubMed: 547472]
- Krauzlis RJ, Basso MA, Wurtz RH. Shared motor error for multiple eye movements. *Science* 1997;276:1693–1695. [PubMed: 9180078]
- Krauzlis RJ, Lisberger SG. Temporal properties of visual motion signals for the initiation of smooth pursuit eye movements in monkeys. *J Neurophysiol* 1994a;72:150–162. [PubMed: 7965001]
- Krauzlis RJ, Lisberger SG. A model of visually-guided smooth pursuit eye movements based on behavioral observations. *J Comp Neurosci* 1994b;1:265–283.
- Krauzlis RJ, Miles FA. Transitions between pursuit eye movements and fixation in the monkey: dependence on context. *J Neurophysiol* 1996a;76:1622–1638. [PubMed: 8890281]
- Krauzlis RJ, Miles FA. Decreases in the latency of smooth pursuit and saccadic eye movements produced by the “gap paradigm” in the monkey. *Vision Res* 1996b;36:1973–1985. [PubMed: 8759437]
- Lisberger SG. Postsaccadic enhancement of initiation of smooth pursuit eye movements in monkeys. *J Neurophysiol* 1998;79:1918–1930. [PubMed: 9535958]
- Lisberger SG, Morris EJ, Tychsen L. Visual motion processing and sensory-motor integration for smooth pursuit eye movements. *Annu Rev Neurosci* 1987;10:97–129. [PubMed: 3551767]
- Lisberger SG, Movshon JA. Visual motion analysis for pursuit eye movements in area MT of macaque monkeys. *J Neurosci* 1999;19:2224–2246. [PubMed: 10066275]
- Lisberger SG, Westbrook LE. Properties of visual inputs that initiate horizontal smooth pursuit eye movements in monkeys. *J Neurosci* 1985;5:1662–1673. [PubMed: 4009252]

- Morris EJ, Lisberger SG. Different responses to small visual errors during initiation and maintenance of smooth-pursuit eye movements in monkeys. *J Neurophysiol* 1987;58:1351–1369. [PubMed: 3437336]
- Morrow MJ, Lamb NL. Effects of fixation target timing on smooth-pursuit initiation. *Exp Brain Res* 1996;111:262–270. [PubMed: 8891656]
- Newsome WT, Wurtz RH, Dursteler MR, Mikami A. Deficits in visual motion processing following ibotenic acid lesions of the middle temporal visual area of the macaque monkey. *J Neurosci* 1985;5:825–840. [PubMed: 3973698]
- Ogawa T, Fujita M. Velocity profile of smooth pursuit eye movements in humans: pursuit velocity increase linked with the initial saccade occurrence. *Neurosci Res* 1998;31:201–209. [PubMed: 9809665]
- Rashbass C. The relationships between saccadic and smooth tracking eye movements. *J Physiol (Lond)* 1961;159:326–338. [PubMed: 14490422]
- Robinson DA. The mechanics of human smooth pursuit eye movement. *J Physiol (Lond)* 1965;180:569–591. [PubMed: 5846794]
- Schwartz JD, Lisberger SG. Initial tracking conditions modulate the gain of visuo-motor transmission for smooth pursuit eye movements in monkeys. *Vis Neurosci* 1994;11:411–424. [PubMed: 8038118]
- Tanaka M, Fukushima K. Slow eye movement evoked by sudden appearance of a stationary visual stimulus observed in a step-ramp smooth pursuit task in monkey. *Neurosci Res* 1997;29:93–98. [PubMed: 9293497]
- Tanaka M, Fukushima K. Neuronal responses related to smooth pursuit eye movements in the periarculate cortical area of monkeys. *J Neurophysiol* 1998;80:28–47. [PubMed: 9658026]
- Wyatt HJ, Pola J, Lustgarten M. The oculomotor “twitch”—a transient response to target motion. *Exp Brain Res* 1989;76:581–592. [PubMed: 2792247]
- Yang DS, Fitzgibbon EJ, Miles FA. Smooth pursuit eye movements: transient post-saccadic enhancement and suppression by saccadelike shifts of the background in humans. *Soc Neurosci Abstr* 1999;29:1399.

FIG. 1. Schematic diagram of experimental design

A: front view of the screen. Open circles indicate possible cue locations. The filled circle shows a target spot that moved only horizontally. **B:** schematic diagram showing time course of stimulus events. The target spot moved in a step-ramp trajectory with a gap before motion onset. The dark bar shows the position of a visual cue that appeared at an eccentric position during the gap between the offset of the fixation target and the appearance of the tracking target.

FIG. 2. Representative eye movements with and without a cue in the temporal gap between the offset of the fixation target and the appearance of the tracking target

A: gap pursuit trial without a visual cue. *B*: cue appeared at 5° right for 100 ms during the gap. *C*: cue appeared at 5° left. The triangles in *B* and *C* indicate the time of cue onset. The fixation target and tracking target were the same in *A–C*. The gap began at the start of the traces and the tracking target appeared at 5° left and moved rightward at 30°/s. Thus the solid and dashed target velocity traces indicate times when the target was and was not visible. In this and subsequent figures, upward deflections or positive values indicate rightward eye movements. Data were obtained from *monkey KLB*.

FIG. 3. Context specificity of the cue-evoked smooth eye movements

Each graph shows the progression of a single daily experiment and plots eye velocity 80 ms after target motion for individual trials as a function of trial number. *A* and *C*: in the 1st and 3rd pursuit blocks, the target appeared 5° to the right or left and moved either toward or away from the fixation target at 30°/s. In the 2nd block, the target jumped 10° horizontally after a 200-ms gap, then remained stationary for 1–1.5 s. *B* and *D*: the 1st and 2nd blocks presented target motion away and toward the position of fixation. Trial numbers without data points indicate intervals in which no cues were presented. In all 4 graphs, the open and filled symbols plot cue-evoked smooth eye velocity when the cue appeared on the left or right. The thick line near zero eye velocity plots eye velocity 80 ms after the appearance of the tracking or saccade target in trials that did not include a cue, based on moving averages of 15 trials. The vertical dashed lines indicate the beginning of the 2nd and 3rd blocks.

FIG. 4. Time course of cue-evoked smooth eye movement

A and *B*: horizontal eye velocity for target motion away from the position of fixation. The vertical dashed line shows the onset of target motion. Gap duration was either 300 ms (*A*) or 200 ms (*B*). *C* and *D*: smooth eye movements evoked by the cue in trials that did not present a moving target. In all 4 panels, the triangles indicate cue onset. Thick traces show averages of eye velocity obtained from over 15 responses, and fine traces show eye velocity in individual trials.

FIG. 5. Comparison of the latency for the initiation of pursuit and cue-evoked smooth eye movements

A and B: initiation of pursuit for target motion away from the position of fixation in the absence of cues. *C and D:* initiation of pursuit for target motion toward the position of fixation in the absence of cues. *E and F:* initiation of pursuit for rightward target motion after cues presented on the left or right. Bold traces show averages of eye velocity for rightward and leftward target motion, and fine traces show eye velocity from individual trials of rightward target motion. Vertical dashed lines show the time of the initiation of pursuit for target motion away from the position of fixation. Triangles in *E* and *F* show the time of cue onset.

FIG. 6. Effects of gap duration on the size of the cue-evoked smooth eye movements

Eye velocity was measured either 80 ms (A and C) or 100 ms (B and D) after target motion onset. The open and filled symbols plot data for rightward and leftward target motion. Points are connected or unconnected depending on whether the trials did or did not include a cue. Error bars indicate 1 SD. Points connected by dashed vs. solid traces show data for cues presented on the left and right, respectively.

FIG. 7. Effect of varying the time of onset of the cue on the amplitude of the cue-evoked smooth eye velocity

A: time course of average eye velocity for rightward target motion toward the position of fixation at $30^\circ/\text{s}$ with different timing of the cues. The triangles indicate cue onset and the numbers at the left of each trace indicate the cue-lead time. The bold trace labeled “NoCue” shows average eye velocity for trials that did not include a cue. The 2 vertical dashed lines show the start and end of a 200-ms gap. The vertical solid lines indicate the onset of pursuit measured from trials that did not deliver a cue. **B:** plots of cue-evoked smooth eye velocity as a function of cue-lead time. From *top to bottom*, data were taken from *monkeys SSK, KRS, and KLB*, all for target motion toward the position of fixation. Measurements were made 180 or 200 ms after the onset of the cue. Filled and open symbols show responses for leftward and rightward pursuit. Dashed and solid lines connect points for responses to cues presented on the right and left of fixation. Error bars indicate 1 SD.

FIG. 8. Effects of cue location and subsequent target velocity on the size of cue-evoked smooth eye movements

A and C: each graph plots averages of eye velocity as a function of cue location. Eye velocity was measured at 80 ms after target motion onset. Data points connected by lines are the responses to a cue presented along the horizontal axis. Unconnected symbols at the right of each panel plot smooth eye velocity evoked in the control noncue trials (NoCue) or with a cue above or below the fixation target (5°v or 10°v). A cue was presented for 100 ms at the start of a 200-ms gap between fixation target offset and tracking target onset. Target velocity was $30^\circ/\text{s}$. B and D: the magnitude of cue-evoked smooth eye movements is plotted as a function of subsequent target velocity. Data were obtained from 4 blocks of trials, which provided target motion at 10, 20, 30, or $40^\circ/\text{s}$. Dashed and solid lines connect points for responses to cues presented on the right and left of fixation. Unconnected points show responses measured at the same times from trials that did not deliver a cue. In all 4 graphs, filled and open symbols show responses for leftward and rightward pursuit. Error bars indicate 1 SD.

FIG. 9. Distributions of the size of cue-evoked smooth eye velocity for trials that presented bilateral cues (A and B) and unilateral cues (C and D)

Eye velocity was measured 80 ms after the appearance of the tracking target. A and B: the histograms shown by solid outlines report the distribution of eye velocities in trials that did not contain cues. The continuous and dashed curves show the predictions for vector averaging and vector summation of the responses to left and right cues alone. C and D: the filled and open histograms show the distribution of the responses to cues present to the right or left of fixation.

FIG. 10. Enhancement of the initiation of pursuit by bilateral cues

A: data from 2 monkeys showing the time course of pursuit initiation. Solid and dashed traces show averages of eye velocity at the initiation of pursuit for target motion in the absence or presence of bilateral cues. For each monkey, the *top* and *bottom pairs of traces* show results for target motion toward or away from the position of fixation. Open triangles indicate the onset of target motion. B: quantitative analysis of the effect of bilateral cues on eye acceleration in the 1st 80 ms after the initiation of pursuit. Pairs of connected points were obtained from no-cue (NC) and bilateral-cue (BC) trials in the same experiments, and different sets of connected points indicate data obtained in different daily experiments. Dashed lines connect values of eye acceleration measured from presaccadic intervals of <40 ms. Asterisks indicate differences that were statistically significant at $P < 0.05$ (*) or $P < 0.01$ (**) levels (paired t -test).

FIG. 11. Enhancement of the initiation of pursuit by bilateral cues for target motion that started at the position of fixation

A and B: averages of eye velocity as a function of time for 2 monkeys. Solid and dashed traces show responses to target motion in trials that delivered bilateral cues or no cues in the absence of a temporal gap interval. The fine dotted traces show eye velocity evoked by target motion toward the position of fixation in the absence of a cue. The open triangles indicate the onset of target motion. Target velocity was always $30^\circ/\text{s}$. The histograms inset at the left of A and B show distributions of eye velocity measured 80 ms after the onset of rightward target motion with bilateral cues. C and D: quantitative analysis of eye acceleration during pursuit initiation. Trios of connected points show data obtained from each daily experiment. Conditions are indicated by the abbreviations along the abscissae: NC-N, targets that started at the position of fixation without a cue; BC-N, targets that started at the position of fixation with bilateral cues; NC-T, targets that started 5° eccentric and moved toward the position of fixation without a cue. In C and D, the 2 graphs show responses for rightward and leftward target motion.

FIG. 12. Analysis of enhancement of the initiation of pursuit after unilateral cues in 2 monkeys
 For each monkey, the *left column of traces* plots the time course of average eye velocity for rightward target motion. Bold, fine, and dashed traces show the responses to target motion after a unilateral cue, target motion in the absence of the cue, and a cue in the absence of subsequent target motion, respectively. The open triangles indicate the onset of target motion. In the *right columns*, the dashed traces repeat the time courses of eye velocity for target motion in the absence of a cue, and bold traces show the difference eye velocity computed as the response to target motion after a cue minus the response to the cue alone.

FIG. 13. A model of the pursuit system with a gain control

The *top pathway* shows visuomotor drive in retinal coordinates, and the *bottom pathway* shows a gain controller that receives both retinal and extra-retinal inputs. The dashed arrows and times in milliseconds indicate the approximate processing delays for visual control of visuomotor drive and of pursuit gain.

TABLE 1

Quantitative summary of the amplitude of the cue-evoked eye movements for all five monkeys

Monkey	Cue Condition		
	None	Right	Left
<i>KLB</i>	-0.02 ± 0.23	-3.15 ± 0.89	4.75 ± 1.21
<i>NNK</i>	0.06 ± 0.08	-2.90 ± 0.80	2.58 ± 1.28
<i>PCK</i>	-0.17 ± 0.07	-2.00 ± 0.23	1.15 ± 0.05
<i>KRS</i>	-0.31 ± 0.29	-5.51 ± 0.44	5.30 ± 1.22
<i>SSK</i>	0.43 ± 0.29	-5.06 ± 0.39	6.05 ± 0.42

Values are means $\pm$ SD, averaged across multiple experiments.