Effects of Lesions of the Oculomotor Cerebellar Vermis on Eye Movements in Primate: Smooth Pursuit

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Takagi, Mineo, David S. Zee, and Rafael J. Tamargo. Effects of lesions of the oculomotor cerebellar vermis on eye movements in primate: smooth pursuit. J. Neurophysiol. 83: 2047–2062, 2000. We studied the effects on smooth pursuit eye movements of ablation of the dorsal cerebellar vermis (lesions centered on lobules VI and VII) in three monkeys in which the cerebellar nuclei were spared. Following the lesion the latencies to pursuit initiation were unchanged. Monkeys showed a small decrease (up to 15%) in gain during triangular-wave tracking. More striking were changes in the dynamic properties of pursuit as determined in the open-loop period (the 1st 100 ms) of smooth tracking. Changes included a decrease in peak eye acceleration (e.g., in one monkey from ~650°/s2, prelesion to ~220–380°/s2, postlesion) and a decrease in the velocity at the end of the open-loop period [e.g., in another monkey from a gain (eye velocity/target velocity at 100 ms of tracking) of 0.93, prelesion to 0.53, postlesion]. In individual monkeys, the pattern of deficits in the open-loop period of pursuit was usually comparable to that of saccades, especially when comparing the changes in the acceleration of pursuit to the changes in the velocity of saccades. These findings support the hypothesis that saccades and the open-loop period of pursuit are controlled by the cerebellar vermis in an analogous way. Saccades could be generated by eye velocity commands to bring the eyes to a certain position and pursuit by eye acceleration commands to bring the eyes toward a certain velocity. On the other hand, changes in gain during triangular-wave tracking did not correlate with either the saccade or the open-loop pursuit deficits, implying different contributions of the oculomotor vermis to the open loop and to the sustained portions of pursuit tracking. Finally, in a pursuit adaptation paradigm (×0.5 or ×2, calling for a halving or doubling of eye velocity, respectively) intact animals could adaptively adjust eye acceleration in the open-loop period. The main pattern of change was a decrease in peak acceleration for ×0.5 training and an increase in the duration of peak acceleration for ×2 training. Following the lesion in the oculomotor vermis, this adaptive capability was impaired. In conclusion, as for saccades, the oculomotor vermis plays a critical role both in the immediate on-line and in the short-term adaptive control of pursuit.

INTRODUCTION

A role for the cerebellum in the control of pursuit eye movements was first identified in the pioneering experiments of Westheimer and Blair (1973) and Burde et al. (1975), who described failure of smooth following in totally cerebellectomized monkeys. Human patients with lesions of the cerebellum also show defects in the generation of pursuit eye movements (Büttner and Straube 1995; Büttner et al. 1994; Lewis and Zee 1993; Straube et al. 1997; Vahedi et al. 1995). Based on the anatomic projections to the cerebellum from areas within the pons that are concerned with pursuit (Glickstein et al. 1994; Nagao et al. 1997; Thierlert and Thier 1993; Yamada and Noda 1987), and the effects of focal lesions within the cerebellum of monkeys, two specific regions of the cerebellar cortex have been implicated in the control of pursuit: the cerebellar foli- culus and paraflocculus (Zee et al. 1981), and the dorsal and posterior cerebellar vermis including lobules VI, VII (Keller 1988), and the uvula (Heinen and Keller 1996). Furthermore, lesions within the portion of the fastigial nucleus that receives projections from Purkinje cells of the dorsal vermis, the so-called fastigial oculomotor region (FOR), also affect pursuit (Ohtsuka et al. 1994; Robinson et al. 1997). Recently, the ventrolateral portion of the posterior interposed nucleus (Robinson and Brettler 1998) and the lateral cerebellar hemispheres (Straube et al. 1997) have also been implicated in pursuit. The finding that multiple areas within the cerebellum are involved in pursuit is unexplained.

In an attempt to unravel the cerebellar contribution to pursuit eye movements, we studied the effects of lesions of the dorsal vermis on pursuit in monkeys. We also studied adaptive capability in the pursuit system, using a short-term learning paradigm analogous to that used for the adaptive control of the amplitude of saccades. Because the animals reported here were also used in a study of the effect of dorsal vermis lesions on saccades (Takagi et al. 1998), we compared the effects of lesions on pursuit with those on saccades. Preliminary reports of some of these results were presented at the Association for Research in Vision and Ophthalmology (Takagi et al. 1996a) and the Society for Neuroscience (Takagi et al. 1996b).

METHODS

General experimental procedures and recording of eye movements

The general experimental procedures and the details of methods of recording eye movements have been described in the previous report that was based on the same three monkeys (Takagi et al. 1998). In brief, the magnetic-field search coil technique was used with coils implanted in both eyes. The output signal from the phase detectors was filtered with a bandwidth of 0–90 Hz, sampled by a digital computer at 500 Hz with 12-bit resolution, and then stored to disk for later off-line analysis. System noise limited resolution to ~0.05°. The coil signal was calibrated by requiring the animal to fix successively on targets at 2.5° intervals over a range of ±25° horizontal and
Stimulus presentation

Target stimuli were under computer control and displayed on a video monitor located 33 cm in front of the monkey, in an otherwise dark room. To elicit pursuit movements we used a step-ramp stimulus in which the target (a square, 3.2° on a side) was displaced eccentrically (4–12°, depending on target speed and the saccade latency of the monkey) and then moved back at a constant velocity toward and then beyond the initial straight-ahead target position. The ramp target crossed the center at 180 ms (monkey 1), 220 ms (monkey 2), and 200 ms (monkey 3) after the onset of target motion. In this way saccades were eliminated in the initial portion of pursuit tracking. In some blocks of trials, the target continued on until it went off the screen. The direction and timing of the stimulus onset were randomized. The latency of pursuit and the acceleration of the eye in the open-loop period were calculated from these trials. Pursuit adaptation was elicited using a double-step of velocity, analogous to the double step of position used for saccade adaptation. After the initial step-ramp of target motion, the target speed was doubled (×2) or halved (×0.5) in speed as it crossed the straight-ahead position. The initial target velocities were 20 and 40°/s. The adaptation paradigms were run as trials of all increasing or all decreasing stimuli, but the directions and amplitudes of target motion were randomized. One hundred trials of each stimulus were elicited.

Data analysis

Analysis was performed using the interactive marking program described in the previous publication (Takagi et al. 1998). Velocity was computed with a digital filter with a 3-dB point at 112 Hz. Pursuit onset was taken when smooth eye velocity reached 2°/s in the direction of the target ramp. Pursuit latency was the difference between the time when the target began to move and the velocity of the eye reached the threshold value. For displaying of individual traces, eye position data were processed in Matlab in which eye position traces were successively filtered (3 db, 30 Hz) and differentiated to produce eye velocity and eye acceleration. Pursuit gain (eye velocity/target velocity) during triangular-wave tracking was based on the average value of the median eye velocity taken from 10–12 sustained epochs.
when the animal was tracking the target well, i.e., keeping its eye position within a window of ±2–3° around the target.

Cerebellar lesions

The cerebellum was lesioned under pentobarbital sodium anesthesia using aseptic techniques. The midline of the dorsal cerebellum was exposed through a suboccipital approach, and a lesion centering around lobules VI–VII was made by bipolar cauterization and aspiration. Corticosteroids and antibiotics were administrated for a week after the surgery. Monkeys showed no defects in their general neurological performance, and recording of eye movements was initiated within the first week after surgery. Details of the techniques for the histological examination and the reconstruction of the extent of lesions are described in our previous publication (Takagi et al. 1998).

RESULTS

Extent of lesions

Figure 1, A and B, shows the reconstruction of the lesions based on histological examination, with the sagittal extent of the lesions being referenced to the bottom of Fig. 1B. The black areas reflect either absence of tissue or areas in which neurons appeared destroyed or white matter disrupted. For monkey 2
Fig. 1A), the lesion was nearly symmetrical, being deepest in the midline where lobules VII and VIII were completely lesioned. Lobules VI and IX were partially involved. The lesion extended laterally to section 3 on both sides, just encroaching on the simple lobule. The lateral component of the lesion on the left side was slightly more extensive (compare left and right sides in sections L3 and R3). For monkey 2 (Fig. 1A), near the midline, lobules VI–VIII were lesioned on both sides, although the lesion was deeper on the right at the R1 level. The lesion, however, extended slightly more laterally on the left side. For monkey 3 (Fig. 1B), on the midline, lobule VII was completely lesioned, but there was mild sparing in lobule VI and moderate sparing in lobule VIII. Both near the midline and more laterally, the lesion was more extensive on the right side and reached the paravermis. In all three monkeys the cerebellar deep nuclei were spared including the posterior portion of the fastigial nucleus. Only in monkey 1 was there some gliosis at the very posterior tip of the fastigial nucleus, although the neurons appeared intact.

General pursuit behavior

Both before and after surgery all animals could hold fixation steadily without spontaneous nystagmus and had no difficulties holding eccentric positions of gaze. There was no spontaneous nystagmus in darkness apart from the low-amplitude drift that many intact rhesus monkeys show. Figure 2 shows a typical example, from monkey 2, of horizontal tracking of a target moving at 20°/s in a triangular-wave pattern, pre- and postlesion. Following the lesion (Fig. 2, right), there was a relatively mild deficit in sustained tracking as reflected in the occasional catch-up saccade, but also a tendency to avoid going to the extremes of eccentric gaze, in this case, more so to the right. The pattern of tracking was qualitatively similar in the other two animals.

Quantitative data for gain during the sustained portion of triangular-wave horizontal tracking are shown in Fig. 3. Note that deficits in gain were relatively small and bilateral for all animals, but for monkeys 2 and 3 they were slightly greater and more enduring for leftward tracking. The decrease in gain tended to be greater for higher target velocities. The maximum percentage decrease after the lesion was 15%. For vertical tracking, there were no consistent changes in gain in any monkey.

Pursuit latencies for horizontal movements in the step-ramp paradigm ranged between 137 and 162 ms and were unchanged following the lesion. For vertical tracking, there were only a few trial types in which there were small
(usually a decrease) but significant changes in pursuit latency following the lesion.

**Pursuit metrics during the open-loop period**

**Pursuit acceleration during step-ramp tracking.** To examine the open-loop, initial period of pursuit, we used the step-ramp stimulus to eliminate any saccades during the early phase of tracking. Figure 4 shows the pre- and postlesion responses for monkey 3 for leftward tracking at 40°/s. Responses were aligned on the target step. Postlesion, there was an inability to sustain eye acceleration during the latter portion of the open-loop period leading to a slower rise toward the final eye velocity. The transient overshoot in eye velocity during the open-loop period that occurred prelesion was absent following the lesion. In this animal, a small initial eye velocity toward the target step appeared postlesion. Finally, eye velocity was not well sustained as the target moved eccentrically.

Figure 5 shows average traces (10 trials) for leftward tracking for velocity (A) and acceleration (B) for all three monkeys at all three speeds. For monkey 3, prelesion, the maximum value of acceleration (Fig. 5B) increased slightly with target speed (275°/s² for a 20°/s stimulus, to 430°/s² for a 60°/s stimulus), and higher values were sustained longer with higher target speeds (from 50 ms at the lower speeds to 100 ms at the high speed). The overall duration of the acceleration period increased slightly with the higher target speed, from \( \sim \)175 to 200 ms. After the lesion, there was little change in peak eye acceleration. At \( \sim \)40 ms after the onset of tracking (when eye velocity was between 12 and 17°/s), the pre- and postlesion velocity traces began to diverge. This was because peak eye acceleration could not be sustained, with maximum values being held only for \( \sim \)40–50 ms. This resulted in a delayed rise to peak eye velocity, which was particularly prominent for the 40°/s stimulus. Note also that the deceleration toward the end of the open-loop period was not as prominent postlesion, and the overshoot in eye velocity seen prelesion at the lower target speeds was no longer evident. Nevertheless, following the initial period of eye acceleration, eye velocity eventually reached target velocity, both pre- and postlesion. For rightward tracking, there was an increase in peak eye acceleration postlesion, but it was not well sustained (shown later in Fig. 13). Consequently, following the lesion, eye velocity no longer transiently overshot target velocity except at the lowest target speed.

For monkey 2, prelesion, the maximum values of eye acceleration ranged between 600 and 700°/s² (Fig. 5B, middle row). The duration of the acceleration period was nearly constant, ranging between 70 and 80 ms, leading to a brief flattening or reversal of the velocity trace that occurred at every target speed, and at almost exactly the same eye velocity, \( \sim \)25°/s (Fig. 5A, middle row). To bring eye velocity up to that of the target at higher speeds, however, there was an additional acceleration, beginning at \( \sim \)100 ms after smooth tracking had begun (possibly driven by visual feedback, just after the end of the open-loop period) and extending over an additional 100–150 ms until target speed was reached. After the lesion, the maximum value of eye acceleration was decreased to 30–50% of the prelesion value. Acceleration tended to be more sustained, however, and the
brief reversal of eye acceleration during the open-loop period, seen prelesion, was no longer present. This pattern made it possible to still reach target speed relatively quickly, even though the initial eye acceleration was diminished. A similar pattern was seen for rightward tracking; postlesion, peak acceleration was decreased but acceleration was more sustained in the latter part of the open-loop period to help the eye reach target velocity (shown later in Fig. 13).

For monkey 1, prelesion, because of technical reasons, there was no comparable set of trials for averaging and illustration in this paradigm. Accordingly, here we show early postlesion data (post, 7 days), and used late (101 days) postlesion data as a substitute for the control data. Immediately postlesion, the maximum values of eye acceleration and the duration of the acceleration period were nearly constant for all target speeds. The maximum value of eye acceleration was just over 200°/s², and the duration was \( \approx 65 \) ms. There also was a plateau in eye velocity, well below target velocity, that occurred after the initial eye acceleration and lasted until \( \approx 180–200 \) ms after pursuit had begun (arrowhead). The plateau decreased in duration with target speed, commensurate with the increase in the duration of eye acceleration as target speed increased. The plateau probably ended when visual feedback became sufficiently available to signal a need for an increase in eye velocity to reach target velocity. Note also that for the 60°/s stimulus, eye velocity did not reach target velocity.

To quantify the data further for monkeys 2 and 3, we measured the average acceleration over the entire 100 ms of tracking during the open-loop period (Fig. 6), and then further subdivided the open-loop period into smaller epochs of 0–20, 20–40, and 40–100 ms (Fig. 7, for 40°/s stimuli). For monkey 3 there was a clear decrease in the average acceleration over the entire open-loop period, more so for leftward than for rightward tracking. The decrease was largely due to the inability to sustain eye acceleration in the later portions of the open-loop period (Fig. 5B, bottom row, and Fig. 7). For monkey 2, the changes in the average acceleration of the entire open-loop period were relatively small. The average trace in Fig. 5, however, showed a deficit in the early portion of the open-loop period, with a relative increase in acceleration in the later portion of the open-loop period. This can also be seen clearly in the data shown in Fig. 7. For monkey 1, prelesion values had to be obtained from the early trials in the adaptation paradigm. Nevertheless, there was a clear drop in average

**Fig. 5.** Tracking to a step-ramp stimulus for all 3 monkeys, at all 3 tracking speeds, in the leftward direction. In A are shown velocities and in B accelerations. For monkeys 2 and 3 (M2 and M3) pre (control) and postlesion data (day 12 for M2 and day 3 for M3) are shown. For monkey 1 (M1) early (7 days) and late (101 days) postlesion are shown, using the late postlesion data as the control because the prelesion data were unavailable. Ten consecutive trials were aligned and then averaged. Thin arrows indicate 100 ms after the onset of tracking, and their placement was based on the velocity traces. There were defects, seen to varying degrees in different monkeys, in both the amplitude of peak eye acceleration and its duration. Postlesion deficits are further discussed in the text. For monkey 1 (M1), the arrowhead indicates the plateau in eye velocity.
acceleration, which for this monkey was apparent at all target speeds.

There was some recovery in the late postlesion period. Figures 3, 6, and 7 also show data from recordings later, usually 2–3 mo, after the lesion. For steady-state gain during triangular-wave tracking, there was a modest degree of recovery for monkeys 1 and 2, primarily for rightward tracking. For eye acceleration in the open-loop period, only monkey 1 showed a consistent pattern of mild recovery, in both directions of tracking.

Vertical pursuit was quantified in monkeys 2 and 3, and, in contrast to horizontal pursuit, we found no decrease in eye acceleration in the open-loop period postlesion. For downward tracking, for just a few trial types (60°/s for monkey 2 and 20°/s for monkey 3), there was an increase in average eye acceleration during the open-loop period, ranging from 50 to 85%.

Pursuit adaptation

Short-term adaptation of pursuit was investigated using a paradigm with a double step of velocity to induce a change in eye acceleration during the open-loop period. Figure 8, left column, shows sample traces of responses of monkey 3 to consecutive trials in the gain-increase (×2) paradigm, pre- and postlesion. Prelesion (left panels), there was an increase in the initial pursuit response with training. Figure 9 shows the average velocity trace for 12 trials during the early and during the late phases of the pursuit adaptation paradigm for monkey 3. Prelesion (Fig. 9, left panel), there is a clear adaptive response, although in this case only after the first ~20–30 ms of pursuit tracking, which was not modified. Figure 10 shows the response to the increasing (×2) and decreasing (×0.5) adaptation stimuli at a target speed of 20°/s for leftward (A) and 40°/s for rightward (B) tracking. Velocity and acceleration traces, pre- and posttraining, are shown for monkeys 2 and 3. Note that for the response in the ×2 adaptation paradigm, the major change is an increase in the duration of the acceleration period. For the ×0.5 adaptation paradigm, the major change is a decrease in the amplitude of peak acceleration. Note that for monkey 2 the earliest ~20–30 ms of pursuit tracking was relatively unchanged, but there was a small change for monkey 3. Following the lesion, the ability to alter eye acceleration adaptively in the open-loop period was severely impaired. For example, monkey 3 could not follow the double step of target velocity without catch-up saccades (Fig. 8, right). This finding is also reflected in the average traces for monkey 3 in Fig. 9, right. Postlesion, training induced little change in eye acceleration during the open-loop period. The traces only separate when information from visual feedback became available (>100 ms after tracking onset) to adjust the ongoing eye tracking movement.

Individual trials throughout the pursuit adaptation paradigm are shown in Fig. 11 for monkey 3 during leftward tracking in the gain-increase paradigm. Note that the adaptive increase in the average value of acceleration in the first 100 ms is dimin-
FIG. 7. Eye acceleration during 3 different epochs (0–20, 20–40, and 40–100 ms) of the open-loop period of pursuit for monkeys 2 (M2) and 3 (M3). Data were obtained as described in the legend of Fig. 5 for plotting of average traces. Leftward tracking for 40°/s step-ramp target motion is shown. For monkey 2, note the decrease in average acceleration in the early epochs (<40 ms) and the relative increase in the later portion of the open-loop period. For monkey 3, there was little change in the first epochs of acceleration postlesion; the main change was a decrease in acceleration in the later epoch (>40 ms). Using the Kruskal-Wallis 1-way ANOVA on ranks and Dunn’s method, there was a significant difference (P < 0.05) between the pre- and postlesion data set when shown by an asterisk.
ished after the lesion. A more extensive quantitative analysis of pursuit adaptation is depicted in Fig. 12 for monkeys 2 and 3. There was a decrease but not an absence of a capability for adaptive modulation of eye acceleration in the open-loop period of pursuit. The deficits were to some extent bidirectional. There was a variable, small recovery of adaptive capability, but in general the deficits were enduring.

For monkey 1, the data before and after each training session were less complete, but this animal also showed deficits in pursuit adaptation. For example, in the ×0.5 paradigm there was a bidirectional decrease in average acceleration in the first 100 ms of tracking at the higher target speed (from a 51% to a 28% change for leftward tracking and from a 62% to a 24% change for rightward tracking).

DISCUSSION

The main finding of this study is that lesions restricted to the dorsal vermis of the cerebellum (“the oculomotor vermis”) impair smooth pursuit performance, with small changes in the steady-state gain triangular-wave tracking and more marked changes in the pattern of eye acceleration during the first 100 ms (the “open-loop” period) of pursuit. We also found that in paradigms calling for adaptive modification of pursuit performance, there was an impaired ability to modify acceleration in the open-loop period of pursuit. These effects on pursuit and pursuit adaptation were independent of any structural damage to the deep cerebellar nuclei, implicating the cerebellar vermis directly both in the immediate, on-line, and in the short-term, adaptive control of pursuit.

Schema for the control of pursuit by the oculomotor vermis

RESULTS OF EXPERIMENTAL STIMULATION AND OF SINGLE-UNIT RECORDINGS IN THE FASTIGIAL OCULOMOTOR REGION (FOR) AND IN THE OCULOMOTOR VERMIS. Many Purkinje cells in the oculomotor vermis discharge in relation to pursuit (Sato and Noda 1992; Suzuki and Keller 1988a,b), with a majority having their preferred direction contralaterally. Some cells in the dorsal vermis carry a signal related to motion of images on the
retina, allowing for reconstruction of the velocity of the target in space (i.e., relative to the head). Experimental stimulation in the dorsal vermis usually decelerates or reverses contraversive pursuit (Krauzlis and Miles 1998). In humans, transcranial magnetic stimulation over the posterior cerebellar vermis accelerates ipsiversive pursuit and decelerates contraversive pursuit (Ohtsuka and Enoki 1998).

In the posterior fastigial nucleus (FOR) Fuchs et al. (1994) have recorded from neurons that discharge in relation to pursuit. Most such cells also discharge steadily during fixation. During step-ramp tracking in the preferred direction (usually contralateral), the most frequently encountered neurons show a burst of activity that begins in advance of contralateral eye acceleration and usually ends before maximum eye velocity is reached. Some of these neurons also show a late burst during tracking in the ipsilateral direction. The pattern of activity during sinusoidal tracking was such that they are maximally active during contralateral eye acceleration or ipsilateral eye deceleration.

CONCEPTUAL SCHEME FOR INITIATION OF PURSUIT: EFFECT OF LESIONS OF THE OCULOMOTOR VERMIS. Fuchs et al. (1994) suggested that the FOR is poised to help accelerate the eyes during contralateral pursuit and decelerate them during ipsilateral pursuit. More specifically, in the context of the response to the step-ramp stimulus, activity in the FOR could influence the open-loop (1st 100 ms) period of pursuit by increasing the discharge in different sets of neurons at different times in the open-loop period. Those cells that start discharging during the very beginning of the open-loop period could facilitate contralateral pursuit acceleration, and those that increase their discharge toward the end of the initial period could help stop ipsilateral acceleration.

Because the output of the Purkinje cells of the oculomotor vermis inhibits the FOR, a bilateral lesion of the oculomotor vermis would be expected to release activity of FOR neurons, both to facilitate the initiation of contralateral pursuit and to inhibit eye acceleration in the later portions of the open-loop period of ipsilateral pursuit. We found that the very initial 20-ms portion of eye acceleration during pursuit could be affected by the lesion in the vermis, especially for leftward tracking in monkey 2 and rightward tracking in monkey 3, but the effect was not as marked as in subsequent portions of the open-loop period. This dissociation could be because the oculomotor vermis has a relatively smaller effect on cells in the FOR when they are discharging in the very early rather than in subsequent portions of the open-loop period of tracking. In this case, the neurons in the FOR that help to end the acceleration period (for ipsilateral pursuit) would be more affected by the absence of Purkinje cell inhibition. The FOR neurons then could increase their “inhibitory” effect on ipsilateral pursuit acceleration and so decrease the duration and/or the maximum value of peak acceleration during the open-loop period.

FIG. 9. Profile of velocity (average of 10 consecutive trials) in response to the step-ramp stimulus, during the early and late portions of the training period (×2, velocity-increasing paradigm), before (left panel) and after (right panel) the lesion for monkey 3 (M3). Note that during the later portion of the training period, the divergence of the velocity traces occurs much earlier before the lesion than after, reflecting the presence of better adaptation before than after the lesion. Note that postlesion the initial velocity toward the position step became more prominent late in the adaptation trials. Arrows indicate 100 ms after the onset of pursuit tracking in the direction of the target.
FIG. 10. Changes in the dynamic properties of the open-loop period of tracking after ×2 (double velocity) and ×0.5 (half velocity) adaptive training for monkeys 2 (M2) and 3 (M3). Eye velocity and eye acceleration are shown for leftward (A) and rightward (B) tracking. Initial target speed is 20°/s for leftward training and 40°/s for rightward training. Note that with ×2 training the main change is an increase in the duration of peak acceleration. With ×0.5 training the main change is a decrease in the value of peak acceleration.
VARIABILITY IN THE EFFECTS OF VERMAL LESIONS AMONG ANIMALS. The amplitude of peak acceleration during pursuit was affected by the lesion of the vermis to varying degrees, depending on the monkey. For example, during leftward movements, one animal (monkey 2) had a relatively large value of peak acceleration prelesion (~600–700°/s²); postlesion, it showed a marked decrease in peak acceleration to values of ~200–375°/s². Another animal (monkey 3) had a relatively low value of peak acceleration prelesion (~275–430°/s²) and showed more of a change (a decrease) in the duration of peak acceleration, postlesion. For monkey 1, peak acceleration decreased from a maximum value of ~475°/s² prelesion to values of ~175–225°/s² after the lesion. Among all the animals, the values of peak acceleration and the duration of peak acceleration were much closer after than before the lesion. Thus, although the effects of the lesions on individual monkeys were variable, the final level of performance postlesion was more consistent. This finding suggests that some of the seemingly variable effects of the lesions on pursuit in different animals might be due to variability in the effect of the cerebellum on the dynamic properties of their intact pursuit, rather than simply due to differences among animals in the extent of lesions. Robinson et al. (1997) also found variability in the effects of muscimol injections into the FOR of different monkeys, which may reflect the same phenomenon.

Another important finding was noted in the postlesion pattern of pursuit eye acceleration of monkey 2. This animal showed a considerable decrease in the value of peak acceleration early during pursuit initiation, but with a small, relative increase in eye acceleration in the later portion of the open-loop period. Consequently, by the end of the open-loop period, eye velocity almost reached the prelesion value. This finding supports the idea that the posited acceleration command during the initiation of pursuit is under the control of a local feedback loop, perhaps comparable to the local feedback loop postulated for generating the saccade premotor eye velocity command (Robinson et al. 1986). Hence any compromise of eye acceleration during the very beginning of pursuit could be compensated for by this internal feedback loop, which is presumably located in structures apart from the vermis. This finding also emphasizes that measuring the average eye acceleration of the entire open-loop period may not reveal more subtle abnormalities in pursuit acceleration. Rather, the peak value and duration of acceleration and the relative acceleration of the eyes during different epochs of the open-loop period may give better insight into the contributions of the cerebellum to the generation of pursuit eye movement commands.

Common role for the oculomotor vermis in the control of the open-loop characteristics of saccades and pursuit

This schema for pursuit outlined above for the FOR and oculomotor vermis is analogous to the posited role for the FOR and oculomotor vermis in the generation of saccades (Fuchs et al. 1993; Ohtsuka and Noda 1995; Quaia et al. 1999; Takagi et al. 1998). This similarity between pursuit and saccades is seen more clearly if one considers that the initial period of pursuit acceleration is an open-loop eye movement in the same way a saccade is open-loop. With this hypothesis, for saccades, premotor networks would be generating an eye velocity command to bring the eye to a certain position, and for pursuit, an eye acceleration command to bring the eye toward a certain velocity (Krauzlis and Lisberger 1994; Robinson 1975; Robinson et al. 1986). Taking this analogy further, the FOR and the oculomotor vermis could control the dynamic properties of the open-loop period of pursuit (as reflected in eye acceleration) in the same way that it controls the dynamic properties of saccades (as reflected in eye velocity).

We previously reported that for individual monkeys saccade amplitude and saccade dynamics could be affected indepen-
dently by a lesion of the vermis (Takagi et al. 1998). One might then expect that pursuit eye velocity at the end of the open-loop period, which would be analogous to saccade amplitude, might be affected by a lesion of the oculomotor vermis differently than the dynamic properties of open-loop pursuit such as peak acceleration. This was largely true, too, in our animals. For example, looking at the responses to the 20 and 40°/s target stimuli in Fig. 5, for monkey 1, the changes in pursuit eye velocity at the end of the open-loop period were relatively greater than changes in peak eye acceleration, whereas the opposite was true for monkey 2.

**CORRELATION BETWEEN SACCADE AND PURSUIT DEFICITS AMONG ANIMALS.** With the idea that the oculomotor vermis controls the characteristics of saccades and of the open-loop components of pursuit in a similar way, we asked whether there were correlations between the saccade and the open-loop pursuit deficits in individual animals. Although the prelesion pursuit data for monkey 1 was not optimal for scrutinizing the fine structure of pursuit acceleration during the open-loop period, there were clear parallels between the changes in peak saccade velocity and peak pursuit acceleration as the animal recovered. First, following the lesion, for both right and leftward tracking, this animal had the lowest values of both peak eye acceleration during open-loop pursuit and peak eye velocity during saccades. Second, comparing early and late postlesion data, e.g., for 40°/s pursuit target stimuli and 20° saccade amplitude, peak saccade velocity increased from 398 to 641°/s for rightward saccades and from 480 to 616°/s for leftward saccades. Similarly peak pursuit acceleration increased from 143 to 334°/s² for rightward tracking and from 237 to 322°/s² for leftward tracking.

One other obvious finding postlesion was that the animal developed a plateau in eye velocity well below target velocity (Fig. 4, arrowhead). This finding of “hypometric” pursuit at the end of the open-loop period [average gain (eye velocity/target velocity) at the end of the open-loop period over all 3 target...
velocities was 0.46 for rightward tracking and 0.47 for leftward tracking] correlated well with the markedly hypometric saccades [average gain (initial saccade amplitude/target displacement) over all 3 stimulus amplitudes was 0.53 for rightward tracking and 0.55 for leftward tracking] shown by this animal. In contrast to the changes in open-loop pursuit and saccade amplitude, the drop in gain during sustained triangular-wave tracking was much less, to values just under 0.9.

For monkeys 2 and 3, we were able to compare pursuit and saccade dynamics more closely (Fig. 13). First, prelesion, for both directions of tracking, monkey 2 had higher values both for peak velocity for saccades and peak acceleration for pursuit than did monkey 3. Following the lesion, monkey 2 had a relatively larger change in saccade peak velocity than in saccade accuracy. Analogously, for monkey 2 the peak value of eye acceleration during the open-loop period of pursuit decreased much more than did the value of eye velocity at the end of the open-loop period. Just the opposite was true for monkey 3. Following the lesion, monkey 3 had a relatively large decrease in saccade peak velocity, with an actual increase in peak eye acceleration. Likewise, for rightward pursuit in this animal, there was a decrease in the duration of peak acceleration during pursuit, and hence a decrease in the value of eye velocity at the end of the open-loop period, but with an increase in the value of peak pursuit acceleration. For this animal, for rightward tracking, however, there was an exception to the general finding that the effect of the lesion on saccades and the open-loop portion of pursuit was the same; there was no increase in saccade eye velocity comparable to the increase in peak pursuit acceleration. For leftward saccades and pursuit, however, the deficits were more comparable; there was little change in peak saccade velocity and no change in peak eye acceleration during smooth pursuit. For monkeys 2 and 3, as was the case for monkey 1 described above, there were comparable deficits in saccade amplitude and in pursuit velocity at 100 ms of tracking, except for leftward tracking for monkey 2, in which case there were hypermetric saccades for some target amplitudes but not “hypermetric” pursuit at 100 ms. Nevertheless, considering the arbitrariness of 100 ms as the end of the open-loop period and the relatively (compared with monkey 1), small changes in gain for both saccades and pursuit shown by monkeys 2 and 3, the analogy between saccades and the open-loop portion of pursuit held reasonably well. To epitomize, when comparing the dynamic properties of saccades with the open-loop portion of pursuit, both before and after the lesion of the oculomotor vermis, all three animals largely showed analogous behavior.

Finally, the gain during triangular-wave tracking for monkeys 2 and 3 was affected to about the same degree as monkey 1, even though the deficits in open-loop performance were less than those of monkey 1 (compare Figs. 3 and 6). This dissociation indicates that lesions of the oculomotor vermis can affect open-loop and sustained pursuit tracking differently. It may be that a similar functional dissociation may be found with lesions in other parts of the cerebellum that contribute to smooth pursuit.

Relevant to the idea of common control of open-loop pursuit and saccades is the finding that some cells within the dorsal vermis as well as some cells in the fastigial nucleus discharge for both saccades and pursuit (Fuchs et al. 1994; Sato and Noda 1992; Suzuki and Keller 1988b). Furthermore, artificial stimulation in the dorsal vermis can affect ongoing pursuit as well as alter the accuracy of ongoing saccades (Hashimoto and Ohtsuka 1995; Krauzlis and Miles 1998; Ohtsuka and Enoki 1998). Krauzlis and Miles (1998) have suggested that the
Pursuit and the cerebellar oculomotor vermis

The cerebellum adjusts a common error signal that can be used for both saccades and pursuit. The brain stem circuits that might mediate such common processing are not known, although there are many potential sites of convergence (Krauzlis et al. 1997). Of course, it simply may be that the oculomotor vermis contains groups of neurons that have separate functions for saccades and pursuit but are closely intermingled (Sato and Noda 1992). Lesions, then, might produce similar deficits in both types of eye movements simply by the proximity of the relevant neurons. Further physiological studies are needed to test the hypothesis of common control of open-loop pursuit and saccades by the dorsal cerebellar vermis, and whether or not the cerebellum influences common or distinct circuitry in the brain stem.

Pursuit adaptation

Pursuit eye movements, like the vestibuloocular reflex (VOR) and saccades, can be shown to undergo adaptive changes to ensure proper calibration of motor responses to the sensory stimuli that drive them. Even though the pursuit system is under “immediate” visual feedback control, because of the inherent latency in visual processing it is burdened with an obligatory, ~100 ms open-loop period of motor response that must be calibrated to sensory inputs for optimal visuoculomotor function. Pursuit adaptation has been less studied than saccade or VOR adaptation, but both humans and monkeys can undergo adaptive changes both in short-term (minutes to hours) learning paradigms in which the visual target stimulus is artificially manipulated (Carl and Gellman 1986; Fukushima et al. 1996; Kahlon and Lisberger 1996) and in long-term experiments in which, for example, an ocular muscle is paralyzed and the subject is asked to view habitually with the paretic eye (Optican et al. 1985). The ocular following response (a smooth tracking response elicited by a rapid movement of the entire visual field) is probably closely related to pursuit in its underlying physiological substrate, and it too can be shown to undergo adaptive modification (Miles 1997; Miles and Kawano 1986).

As Kahlon and Lisberger (1996) recently reported, our animals, prelesion, were able to adaptively modify average eye acceleration in the open-loop period of pursuit in a paradigm using a double step of velocity. We did notice, however, a seeming difference in the mechanism between adaptive increases and decreases in initial pursuit acceleration. At the relatively high speeds of target motion that we used, adaptive increases in acceleration were usually accomplished by an increase in the duration of the acceleration period, whereas adaptive decreases in acceleration were accomplished by both a decrease in the amplitude and in the duration of peak acceleration. The maximum value of eye acceleration during the open-loop period of pursuit may be relatively limited, especially for high target speeds, necessitating an increase in the duration of the period during which peak eye acceleration is maintained whenever pursuit innervation must be further increased. An analogous situation occurs with saccades. Saccade peak velocity approaches a saturation for large amplitude saccades, and, when adaptation to muscle weakness is required, increases in the size of large saccades are probably accomplished by an increase in the duration rather than in the maximum value of the saccade velocity command (Abel et al. 1978; Scudder 1998).

For both saccades and the VOR there is direct evidence that the cerebellum participates in the mechanisms by which these ocular motor subsystem undergo learning (Cohen et al. 1993; Lisberger et al. 1984; Optican and Robinson 1980; Optican et al. 1986; Raymond et al. 1996; Scudder 1998; Takagi et al. 1998). The evidence for involvement of the cerebellum in pursuit or ocular-following adaptation, however, has until now only been hypothetical (Yamamoto et al. 1998), with no prior direct demonstration. Here, we have shown directly for pursuit, as we did for saccades, that lesions of the oculomotor vermis interfere with ocular motor adaptation. We emphasize again, however, that as for the pursuit deficits themselves, the adaptation deficits were not total. Whether this means that other parts of the oculomotor vermis or other parts of the cerebellar cortex such as the ventral paraflocculus are involved in pursuit adaptation, remains to be shown (Nagao and Kitazawa 1998).

In sum, the cerebellar vermis plays a role in both saccade and pursuit adaptation. This is not unexpected because the inherent requirements for optimal visual motor function in tracking systems that are encumbered by an obligatory visual delay are the same for saccades and pursuit. The “open-loop period” must be accessible to long-term calibration so that eye movements bring the image of the object of interest to the fovea and keep it there, but without producing any motor instability that would interfere with visual function.

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