Chapter 4

Smooth Pursuit and Visual Fixation

THE PURPOSE OF SMOOTH PURSUIT

Smooth pursuit eye movements allow clear vision of objects moving within the visual environment—such as when we watch an eagle soaring in front of cliffs. Dodge pointed out that this ability depends upon the generation of continuous eye movements that “keep the line of regard congruent with the line of interest.” He demonstrated that the velocity of smooth pursuit eye movements matched the velocity of the target; that pursuit had “the character of habitual movements”; that it was...
continuous in nature with no “periods of rest”; and that vision remained clear throughout the movement. To achieve this last attribute, the image of a moving object must be attended to and kept on the fovea. Smeared images of the stationary background that move across the rest of the retina due to the eye movement are ignored, although they may be used to estimate the target’s location in space.64

Although most research on smooth pursuit embodies Dodge’s concept of eye movements that follow moving targets, F. A. Miles has suggested that the system actually evolved to keep the fovea pointed at a stationary target during self-motion.318 As we walk through our environment, we induce an optic flow of images on the retina. The optic flow provides important information about the three-dimensional (3-D) layout of the environment and our direction of heading.8a,19,180 However, excessive slip of images on the retina degrades vision. Smooth pursuit reduces image slip of an object of interest on the fovea, while optic flow still occurs on other parts of the retina. In other words, smooth-pursuit movements must be generated in response to local optic flow on the fovea, but not in response to optic flow on the rest of the retina. Furthermore, other visually mediated eye movements, such as the optokinetic responses to retinal image motion caused by head rotations and translations must be suppressed during smooth pursuit. The implication is that smooth pursuit depends on an ability to compensate for the effects of retinal image motion so that objects are correctly localized in space, and filter out visual motion inputs save for those at the focus of attention.460 Once evolved, such a mechanism could also be used to pursue a small object moving across a complex background, or help to hold the image of a stationary object on the fovea when the observer was stationary—visual fixation. The illusion of motion of the stationary world during pursuit has been reported by a patient with posterior cortical lesions: the patient’s symptom suggested that the mechanism to filter out image motion caused by eye movements had been disrupted.181 Inadequate smooth pursuit is partially compensated by frequent saccades, which re-foveate the object of interest when the eye drifts off target. Nonetheless, patients with impaired smooth pursuit have impaired vision of moving targets.151 Under natural circumstances, we often track moving targets with combined movements of eyes and head; this behavior is discussed in Chapter 7.

**VISUAL FIXATION**

**Gaze Stability with and without Visual Fixation**

To see a stationary object best, its image must be held steadily upon the fovea. As discussed in Chapter 1, visual acuity is influenced by either motion of the image, or displacement of it from the center of the fovea. For clear vision of higher spatial frequencies (e.g., a 20/20 Snellen optotype), motion of the image should be less than about 5 degrees per second and the image should lie within 0.5 degrees of the center of the fovea.69,78,216 However, if images are perfectly stabilized on the retina, vision fades.128,378,420 Visual fading occurs because, like other sensory systems, the visual system habituates its responses to persistent stimuli.304 During natural activities, the major threat to steady fixation comes from perturbations of the head.175 However, even if the subject’s head is stabilized using a bite-bar, gaze is still disrupted by involuntary eye movements.140,249,304,419,420 An example is shown in Figure 4–1. The gaze instability during attempted fixation is more prominent in the torsional than the horizontal or vertical planes.144,356 It has three main components: a high-frequency low-amplitude tremor, small saccades, and slow drifts. The frequency of the tremor ranges up to 150 Hz and its amplitude is less than 0.01 degree, which corresponds to less than the size of one photoreceptor.249,256,412,420 It is uncertain whether ocular tremor aids vision.304 The small saccades, called microsaccades, are typically less than a third of a degree in amplitude, occur in all directions, and follow the main-sequence, like larger saccades.505 Microsaccades can be suppressed during visual tasks that demand steady fixation, such as threading a needle, or sighting a gun.122,420 They may also be influenced by attention shifts.141,152 There has been doubt as to whether microsaccades serve any role for visual perception,304 although some insights have been obtained from electrophysiological studies in primates. Microsaccades do cause bursts of spikes in the lateral geniculate

**Smooth Pursuit and Visual Fixation**
nucleus and primary visual cortex (V1) in monkeys, and the vigor of these bursts is influenced by the properties of the current visual stimulus. Furthermore, psychophysical studies indicate that peripheral vision fades due to habituation when microsaccades are suppressed. Thus, microsaccades may aid vision during fixation, and current research is seeking to clarify their role.

When a subject views a stationary target with the eyes close to center position, the slow drifts that occur during attempted fixation—and the image motion that they produce—are small (standard deviation of position is typically less than 0.1 degrees and of velocity is less than 0.25 degrees per second). When the eyes move away from the central to an eccentric position in the orbit, gaze-evoked nystagmus may develop because stability of gaze becomes susceptible to elastic restoring forces due to the passive properties of the orbital contents; this issue is discussed in Chapter 5. When a subject sits in darkness and attempts to look at the remembered location of a target, the velocity of slow drifts increases about fourfold above that when actually looking at the target (Fig. 4–2). This implies that during vision of the stationary target, any slip of images on the retina due to ocular drifts stimulates the brain to generate eye movements that will counter the drifts, and hold gaze steady. This response to drift of images upon the retina caused by instability of gaze during active fixation has been referred to as slow-control, or a field-holding reflex. Eye drift is especially likely to occur in wake of saccade. Clear vision just after a saccade is critical since, during the saccade, the subject has been mainly blind to what has been happening in the visual world. There is evidence that the field-holding reflex is enhanced at that time. Thus, the ocular follow response to motion of a large textured moving stimulus is increased if motion starts just after a saccade, or during smooth pursuit. These responses occur at ultra-short latencies (about 70 ms in humans) and are not dependent on the subject attending to the visual stimulus. Furthermore, the shortest latency responses occur for images in the plane of fixation (i.e., for binocular images that lack disparity). Thus, these pre-attentive ocular

Figure 4–1. Gaze stability during fixation in a normal subject. The subject was viewing a small, stationary cross at a viewing distance of 1.2 meters in normal room illumination, with head stabilized. Three-dimensional rotations of both eyes were measured using the magnetic search coil technique. Gaze positions are relative, having been offset for clarity of display. RH: right horizontal; LH: left horizontal; RV: right vertical; LV: left vertical; RT: right torsional; LT: left torsional. Positive deflections indicate rightward, upward, and clockwise rotations, from the point of view of the subject. Note that small saccades and drifts occur; the drifts are greater in the torsional plane.

Figure 4–2. Comparison of gaze stability during fixation of a small red target light in a dark room and during attempted fixation of the remembered target location after it had been turned out (indicated by arrow). The subject had been instructed to suppress saccades. Note that increased drift occurs, especially horizontally, after the light is turned out. Conventions are similar to Figure 4–1.
following responses seem admirably suited to stabilize the eyes immediately after saccades and appear to be an important part of a visual fixation mechanism. The question then arises: Is there an independent visual fixation system distinct from smooth pursuit?

Evidence for and against an Independent Fixation System

One line of evidence that fixation differs from smooth pursuit comes from electrophysiological studies in monkeys. Thus, certain parietal lobe neurons discharge during steady fixation but not during smooth pursuit of a moving target. Furthermore, some of these neurons respond to both the presence, or momentary disappearance, of the fixation stimulus. Thus, the parietal lobe seems important in the engagement and disengagement of fixation. Microstimulation of neurons in the pursuit pathway—the medial superior temporal visual area, the dorsolateral pontine nucleus, or the posterior vermis (see Fig. 6–6), produces changes in smooth eye velocity only if the monkey is already engaged in smooth pursuit; it does not produce pursuit if the object of regard is stationary. Thus, there is also electrophysiological evidence for a mechanism to suppress both saccades and pursuit during attempted fixation. Microstimulation of parts of the frontal eye fields and the rostral pole of the superior colliculus will suppress or delay the initiation of a visually triggered saccade. Stimulation of the rostral pole of the superior colliculus, which seems important for fixation, also suppresses ipsilateral smooth-pursuit movements; pharmacological inactivation increases ipsilateral pursuit. Thus, the electrophysiological properties of both the saccadic and the pursuit systems are changed during active fixation of a stationary target, suggesting the influence of an independent, visual fixation system.

There is also evidence from behavioral studies that visual fixation differs from smooth pursuit. Most such studies have focused on differences between smooth pursuit of a moving target, and the eye movements that occur just after the target comes to a halt. In the latter case, retinal image slip is due to eye motion rather than target motion, and the function is therefore equivalent to visual fixation. During smooth pursuit of a moving target, and especially at the onset, small ocular oscillations may occur (Fig. 4–3). These oscillations are usually absent or minor after the target for pursuit comes to a halt (Fig. 4–3), suggesting that different mechanisms are involved in fixation than in pursuit. However, the presence of these oscillations might be due to other experimental factors. For example, oscillations do occur after the target stops if there is uncertainty about whether it will do so or speed up. Thus, the oscillations that occur during smooth pursuit may be because the brain is placing greater reliance on visual inputs, and may not be related to whether retinal slip is due to target or eye motion. Similarly, oscillations are present when patients who have lost vestibular function attempt to view a stationary target while they are rotated at constant speed in a chair; in this situation, visual mechanisms must substitute for the vestibulo-ocular reflex.

Other attempts to identify an independent fixation system have involved comparisons of the dynamic properties of visually mediated eye movements when the eyes are either stationary or engaged in pursuit. First, the latency to onset of express saccades using the gap paradigm (Fig. 3–2B, Chapter 3), in which the fixation light is turned off before the new target is displayed, is approximately the same whether the target is stationary (fixation) or moving (smooth pursuit). Thus, the trigger for these saccades does not recognize the difference between fixation and pursuit. Second, comparison of the ability to visually track a target that vibrates sinusoidally around a stationary target (corresponding to fixation) is no different from the response when similar vibrations that are superimposed upon ramp motion of the target (smooth pursuit). Thus, the tracker for these saccades recognizes the difference between fixation and pursuit. However, a single sine-wave cycle that increases the velocity of a ramp motion does produce a larger response than if the same sine wave is presented during fixation. This latter finding has been interpreted as evidence for on-line control of pursuit gain rather than separate pursuit and fixation systems. A final line of evidence that does support an independent pursuit system is that patients are reported who show normal fixation of a stationary target, but whose eyes break into oscillations of the type seen in congenital nystagmus when they...
Figure 4–3. Initiation of smooth pursuit in response to a 15-degree per second step-ramp (Rashbass) stimulus, showing position (A) and velocity (B) plots of the response. In the velocity record, saccades have been removed. Positive values correspond to rightward movements. Note how, in A, the target (T) initially steps 1.8 degrees to the left (thereby creating a position error on the retina) and then immediately a smooth movement begins to the right at 15 degrees per second (creating a velocity error on the fovea). If the main response of the pursuit system were to the position stimulus, the initial movement would be in the direction of the initial target step (to the left). In fact, the eye (E) commences a smooth pursuit movement in response to the smooth movement of the target (to the right). In B target velocity (T) and eye velocity (E) records correspond to position records A. Target onset is at 0 seconds. After a latency of about 120 ms, the eye accelerates to a peak value (maximum slope) of 140 degrees per second/second. Eye velocity initially overshoots target velocity; thereafter, eye velocity oscillates (“rings”) at a frequency of 2 Hz to 3 Hz. Note that when the target stops, the eye decelerates with a time course that approximates a negative exponential with a time constant of about 90 ms.
try to pursue a moving target (see Video Display: Disorders of Smooth Pursuit). To summarize the evidence: on the one hand, a fixation mechanism has been demonstrated for the suppression of saccades; this depends on known structures, such as the rostral pole of the superior colliculus, and is discussed further in Chapter 3. On the other hand, it is still debated as to whether retinal image motion is reduced by a separate fixation system when the target is stationary and by smooth pursuit when the target is moving. However, the ocular following responses to large textured moving stimuli, which occur at latencies as short as 70 ms, appear to constitute a field-holding visual fixation mechanism. These ocular following responses may also be part of the mechanism that stabilizes the fovea on a stationary target during locomotion. Thus, both ocular following and the translational vestibulo-ocular reflex (VOR) (but not the rotational VOR—see Chapter 2), obey Listing’s law.

STIMULUS FOR SMOOTH PURSUIT

In this section, we first examine attributes of stimuli that have been used to induce visual following eye movements, including smooth pursuit. We then discuss how smooth pursuit can be sustained either with stimuli that do not move or with non-visual stimuli. Finally, we review the role of stimulus predictability in generating the pursuit response.

Effects of Properties of the Visual Stimulus on Visual Following and Smooth Pursuit

GENERAL ASPECTS OF STIMULI THAT INDUCE OCULAR FOLLOWING

Although physics provides no special status for motion, which is simply displacement over time, several lines of evidence support the idea that the brain treats visual motion information separately from visual position information. Perhaps best known is the waterfall illusion. It is induced by staring for some time at a moving object, such as a river or waterfall that occupies a substantial part of the visual field. Stationary objects viewed immediately afterwards in that same part of the visual field appear to move in the opposite direction. Thus, during the waterfall illusion, motion and position are dissociated, since the visual stimulus is seen as moving, and yet it remains in the same position on the retina. The waterfall illusion is not due to eye movements, such as optokinetic after-nystagmus, rather it represents adaptation of the motion-vision system (recall that all sensory systems tend to habituate to persistent stimuli). The other line of evidence for an independent motion-vision system is based on electrophysiological studies that will be reviewed throughout this chapter. What sort of moving visual stimuli can drive smooth-tracking eye movements?

Ocular following responses can be driven by first-order or second-order motion stimuli. First-order motion stimuli are defined by the spatial distribution of luminance. Examples of second-order motion stimuli, which depend on higher-level mechanisms, are contrast and flicker. Routinely, smooth pursuit is tested as subjects track a small spot of light, such as a laser spot projected onto a tangent screen in an otherwise dark room. However, this sort of visual stimulus is impoverished compared to what we see and track during natural activities. By studying ocular following responses to a range of first and second-order visual stimuli, and by pitting first-order against second-order motion, insights have been gained into the mechanisms by which different areas of visual cortex process information on moving stimuli. Thus, the earliest visual following responses occur at latencies as short as 70 ms in response to large, textured moving stimuli; they are not influenced by factors such as attention to the stimulus. As noted above, the ocular following responses are enhanced in the wake of a saccade, and seem well suited to serve as a field-holding visual fixation mechanism. Similar mechanisms probably aid alignment of the eyes; these short-latency disparity vergence responses are described further in Chapter 8. Since primary visual cortex and some secondary visual areas do not respond to second-order visual stimuli, it seems possible that testing patients with these two types of moving stimuli may prove useful diagnostically, an issue that is discussed later in this chapter.
STIMULI FOR SMOOTH PURSUIT

When a small moving spot of light is used to stimulate smooth pursuit, the image of the target may not cover the fovea (it may be smaller); indeed, it may not lie on the fovea, and such parafoveal tracking may be preferred if ambient light is poor, at which time rods are more efficient photoreceptors than cones. Pursuit tracking can also be triggered by objects moving in the far visual periphery and can begin before a saccade can be programmed. Nevertheless, foveal lesions do impair smooth pursuit of small targets.

Experimentally, the responses to stimulation of various parts of the field of vision have been mapped by measuring the initial eye acceleration to targets that are projected onto specific portions of the retina in both humans and monkeys. Each trial starts during fixation of a stationary target so that the retinal location of the moving stimulus can be controlled. The fixation light is then turned out and a moving stimulus appears synchronously in the chosen part of the visual field. Since it takes about 100 ms for a pursuit eye movement to be initiated after the presentation of such stimuli (similar to Fig. 4–3), it follows that the first 100 ms of the pursuit movement will be due to stimulation of the selected portion of the retina. This technique is a sensitive way of measuring the open-loop response of pursuit that occurs before visual feedback is possible. The initial acceleration of the eye in response to horizontal, transient target motion is greater for target motions in the central than in the peripheral field, and is greater for targets moving towards the fovea than for targets moving away from the fovea. For vertical target motions, eye accelerations are greater for stimulus motion in the lower visual field, irrespective of whether the target is moving towards or away from the fovea. Bright targets elicit greater eye accelerations, at shorter latencies, than do dim targets. Attention to the target improves smooth-pursuit performance.

Cues that signal the saliency of a target for smooth pursuit reduce latency to onset, provided they are located in a similar part of the visual field as the pursuit target. Target saliency signaled, for example, by color, has greater effects on pursuit onset when target motion is directed towards the fovea. Stationary distracters placed in the hemifield opposite to the moving target increase the latency to onset of pursuit.

Another technique used to determine the relative influence of different parts of the retina upon smooth pursuit is artificial stabilization of images upon the retina using electronic feedback. For example, if a target is stabilized at the fovea, and optokinetic stimuli are presented to the peripheral visual field, the optokinetic response is partially suppressed. However, the responses to such stimuli are affected not only by the visual stimulus but also by the subject’s mental set. Furthermore, because the moving stimuli are presented to one part of the eccentric retina, there is a displacement, or position-error component to the stimulus. Pursuit responses to target displacements are discussed in the next section.

When a subject pursues a larger stimulus, such as one that almost fills the visual field, the pursuit response is usually enhanced. This may be due, in part, to stimulation of a larger area of retina, but another factor that improves tracking is the freedom to select and attend to any feature of the visual stimulus. When a full-field visual stimulus is used, the central 5–10 degrees of the visual field still dominates the response. As noted above, with sudden movement of full-field visual stimuli, humans generate ocular following responses at latencies as short as 70 ms.

Under natural conditions, we pursue objects that move across a background provided by the stationary environment. As noted at the beginning of this chapter, under these conditions, slip of images of the stationary background occurs on the retina. Thus, a mechanism must exist to at least partly ignore the slip of images of the stationary background and focus attention on the relatively stable image of the moving target. Another feature of natural stimuli for pursuit is that the moving object may be in a different depth plane than the background. When the moving target and the textured background lie in the same depth plane, there is a 10%–20% decrement in pursuit gain compared with tracking the same target in the absence of a background. This effect is more pronounced for the onset of pursuit than during its maintenance, and is influenced by the physical characteristics of the target and
The effect of the background is still present even if it is excluded from the path taken by the target, or seen only by one eye while the other sees only the moving target. If, however, the target moves in a plane that is closer than the background (corresponding to natural conditions), pursuit is improved. Taken together, these findings suggest that, under natural conditions, the smooth-pursuit response depends upon binocular visual inputs to generate a response appropriate to keep the eyes on a target moving through the environment.

If the background on which a small visual stimulus is projected moves—a rare event outside of the laboratory—there is a percept that a small target projected onto it moves in the opposite direction (the Duncker illusion). Further, if a small target moves vertically over a horizontally moving background, subjects experience a strong illusion that the trajectory of the target is diagonal, but smooth pursuit follows the vertical target motion.

This finding illustrates how perception and pursuit can be dissociated, because of the low-level machine-like response of brainstem circuits. Subjects can be tested with more complex moving visual stimuli such as two-dimensional plaids, consisting of two sinusoidal gratings of different orientation. When two orthogonal moving gratings are presented, the ocular tracking response is best predicted by vector averaging of responses to each component grating. However, when plaids are constructed by summing one moving and one stationary grating with 45-degree orientation difference, ocular following shows two components: a shorter-latency response in the direction of grating motion, and, after a further 20 ms, a second component that brings the direction of the response to correspond with pattern motion. Similarly, if subjects track line-figure diamonds, the initial eye movement is a vector average of the diamond's line segments, but the response eventually becomes tracking of the motion of the object. The significance of these dissociated responses is that they have been generated by different functional components of the visual system, perhaps corresponding to the first-order and second-order motion. Such experimental paradigms can be used to better understand motion processing in visual areas of cerebral cortex.

**Influence of Dynamic Properties of the Stimulus on Smooth Pursuit**

What information about the movement of an image of a target does the pursuit system use? Is it target position (where) or target motion (at what speed)? In support of the importance of target motion, Rashbass and later Robinson showed that if a target abruptly jumps (steps) to one side of the fovea and then immediately begins a smooth movement in the opposite direction (a step-ramp stimulus; Figure 4–3), the subject will make a smooth eye movement in the direction of the ramp, but no saccade in the direction of the target step. In other words, the pursuit system responds to the ramp and the step appropriately, taking into account the motion of the ramp, which brings the target back to the fovea and so makes a saccade unnecessary. In fact, cortical areas that abstract visual information about target motion project to both pursuit and saccade-generating mechanisms; this is discussed further in the section on Neural Substrate for Smooth Pursuit.

Although the rate of image motion on the retina is probably most important, particularly in initiating pursuit, there is evidence that the smooth pursuit system may respond to both position and velocity errors. The position error response is much more prominent when the eye is already tracking the target, and when the target jump is oppositely directed to the ongoing response. Furthermore, acceleration of the image of the target upon the retina also serves as a stimulus to pursuit. Additional insights have been gained by studying responses to step-ramp stimuli that change direction; these show responses in which the saccadic component is mainly in response to position error while the pursuit component is principally influenced by target motion. Furthermore, a sudden change in the direction of the stimulus being pursued may serve as a stimulus to pursuit independent from the mechanism determining eye speed.

The interaction between pursuit and saccades has also been studied by simultaneously presenting two targets that move in different directions. Monkeys respond to such stimuli first with a pursuit movement that is the vector average of responses to the two individual target motions. However, after the first
is made towards one of the targets, the pursuit movement is enhanced for movement of that target and suppressed for the other. Furthermore, if a saccade is evoked towards one of the moving targets by microstimulation of the monkey’s frontal eye field or superior colliculus, that target is automatically chosen for subsequent pursuit. These findings suggest that the saccadic command sets the agenda for the subsequent pursuit movement.

Pursuit Responses to Visual Stimuli that Do Not Move and Non-Visual Stimuli

Image motion on the retina is not the only stimulus capable of eliciting smooth pursuit movements. Some subjects can smoothly track their own outstretched finger while in darkness, probably using knowledge of the motor command to the limb (efference) and the consequent proprioceptive input (reafference). Certain patients with acquired blindness can do the same. By four years of age, children can pursue a partially occluded target or strobe-illuminated motion of their own finger. Few individuals can generate smooth eye movements without any perception, or short-term memory, of a moving stimulus. However, most can do so in response to certain second-order visual stimuli, in which no image motion has actually occurred in the direction of the eye movement. Examples of such stimuli are the apparent motion of sigma and phi phenomena and the motion of the imaginary center of a rolling wheel. When subjects smoothly track such apparent motion, the perception of motion and the pursuit eye movements are highly correlated. In normal subjects, the onset and maintenance of smooth pursuit deteriorates as a function of the spatial and temporal separation of flashed stimuli.

A related finding is that patients with cortical lesions causing simultagnosia, defined as difficulty in seeing a single object in the presence of others, can still generate smooth pursuit at a time that they could not report seeing the target. Thus, in addition to direct information about image motion from the retina, the brain can generate pursuit movements by using information about target motion from other sensory systems, by monitoring motor commands and by using higher-level perceptual representations of target motion.

Smooth Pursuit to Predictable Target Motion

The Range of Predictive Pursuit Behavior

Another feature of the stimulus that greatly influences smooth-pursuit stimulus performance is the predictability of the target motion. In nature, both unpredictable movements (e.g., of a predator) and predictable motions (e.g., generated by the subject’s hands) occur and must be pursued. One example of predictive behavior is that the eye will start to move in anticipation before the onset of target motion. These anticipatory drifts are small (less than 1.0 degrees per second) if the time of onset and the direction of target motion are unknown. When the target light is kept on throughout the testing, real or apparent motion of the target is necessary to evoke anticipatory eye movements. However, if the target light is extinguished at the onset of a trial, following several prior, predictable, target motions, anticipatory drifts may increase to over 5 degrees per second. They may be even faster and of short latency if subjects move the target with their own hands. The movements are faster if the anticipatory movement starts from an eccentric eye position and moves centripetally. Once the target starts to move, a predictive acceleration of the eye occurs. For example, if on some trials of a predictable and repetitive nature the target light is extinguished just at the time that it would start to move, the eye may still accelerate. If the target velocity is unexpectedly reduced, eye velocity may exceed it. This behavior cannot depend upon actual motion of the target because that visual information has not yet reached the ocular motor neurons (due to the time taken for visual processing—over 70 ms). There is similar anticipation of the target stopping and of reversal of direction. In monkeys, extinguishing (blinking off) the moving target light is reported to cause a much greater decline of eye velocity than if an occluder is placed in front of the target, a finding requiring confirmation in humans who have been given specific instructions.
Taken together, it appears that anticipatory drifts and early accelerations of the eye depend upon previous tracking experience, a form of memory that depends upon perceived motion. This memory for stimulus motion is not simply limited to one direction or speed, but can extend to generate a series of anticipatory responses, suggesting that velocity information for each can be stored and released in the appropriate order. Thus, if monkeys repeatedly track a target that initially moves horizontally but then changes direction after a predictable period, they will make the direction change even for probe trials, when the target continued to move horizontally. This result suggests that the adapted behavior depends more on timing (duration of horizontal motion) rather than remembering a spatial location. Human subjects can voluntarily stop anticipatory pursuit movements to a cue, and even countermand pursuit movements, similar to what has been described for saccades. Furthermore, the timing of the response to auditory cues, the magnitude of the response itself, and selection of responses to one of two targets, can be independently controlled. The store of memory for anticipatory smooth eye movements may exceed 14 seconds. The same mechanisms appear to generate anticipatory responses during tracking of a visible or imagined head-fixed target during rotation in yaw.

POSSIBLE MECHANISMS FOR PREDICTIVE PROPERTIES OF SMOOTH PURSUIT

After pursuit is initiated, subjects may be able to match almost perfectly the motion of a target moving in a regular waveform, such as a sine wave. This predictive response is established rapidly—as soon as a quarter cycle after the onset of sinusoidal target motion. As discussed below in the section on Models of Smooth Pursuit, this behavior defies explanation by simple models of smooth pursuit that incorporate a delay due to visual processing. Certain unusual waveforms (such as a cubic function or sum of several different sine waves) also can be smoothly tracked, following a training period. Other studies have shown that predictive features of smooth pursuit can be related to performance on the preceding trials. This has led to the suggestions that prediction in smooth pursuit is due to storing of memories of eye movements and referring to them during tracking. However, simply viewing repeated, predictable target motions can promote anticipatory smooth eye movements.

A second possible mechanism, however, is an extrapolation of target behavior based upon the current stimulus to the pursuit system. This is evident if subjects track targets moving at constant speed and, at an unpredictable time, the target light is turned off. Eye velocity falls about 200 ms after the target disappears, but not to zero; the eye continues to move at about 60% of target velocity for periods of up to four seconds. Because the amplitude of this “residual velocity” depended upon the previous target velocity, extrapolation seems likely. Furthermore, the eye will start to speed up again before the target is turned back on, if this is done in a predictable fashion. Although more than one predictive mechanism may aid smooth pursuit, there are differences between those subserving pursuit and predictive mechanisms underlying saccadic tracking. Thus, predictive mechanisms for pursuit are quickly established, whereas observation of several cycles of target jumps is generally required before predictive saccades can be generated.

QUANTITATIVE ASPECTS OF SMOOTH PURSUIT

Having reviewed properties of the stimuli for smooth pursuit, here we summarize methods to quantify responses. Smooth-pursuit performance varies considerably among individuals and is affected by many factors such as the properties of the stimulus, attention, and age. Smooth-pursuit eye movements are sensitive to the effects of many medications (see Table 12–11, Chapter 12). Conventionally, pursuit is measured during tracking of predictable, sinusoidal target motion. There are advantages, however, to measuring the initiation of smooth pursuit and we will start by summarizing the properties of normal responses to such stimuli.

Onset of Pursuit

The initiation of smooth pursuit is most conveniently studied by measuring eye position and velocity in the first second following pres-
entation of either a ramp or a step-ramp (Rashbass) stimulus (Fig. 4–3). The latency to onset of smooth pursuit in response to a ramp target motion is about 100 ms, and is not substantially influenced by turning off a fixation target before a pursuit target appears, in the way that saccades are; thus, using the gap stimulus, there does not appear to be any express smooth pursuit. If the ramp is proceeded by a step displacement in the opposite direction, the latency is greater, close to 150 ms, because the pursuit system is affected by the step stimulus. Nevertheless, such step-ramp stimuli do have an advantage over pure ramp stimuli because they are less likely to stimulate saccades that often contaminate pursuit responses to ramp stimuli.

In humans or monkey, eye acceleration during the initial 40 ms of the pursuit response to a step-ramp stimulus is largely unrelated to the speed of the target, its brightness, or its position in the visual field. Typical values for this initial eye acceleration are 40 degrees per second per second to 100 degrees per second per second, varying from subject to subject. Thereafter, eye acceleration is a function of the velocity of image motion on the retina, and is decreased if the target is dimmer or if it stimulates more peripheral retina. As target velocity is progressively increased, eye acceleration does not increase by the same amount; this has been called acceleration saturation. Thus, the relationship between peak eye acceleration and target velocity is one measure of smooth pursuit initiation. Latency to onset, but not eye acceleration, may be influenced by the presence of a distracter. In monkeys, the initial acceleration, but not latency, of pursuit onset is reduced if targets move across a textured background.

Elderly human subjects show a decrease in initial acceleration, but no change in the latency to onset of pursuit. Infants less than 12 weeks of age do show some pursuit responses; although they are relatively small and intermittent, they may provide a means to estimate visual acuity. By four months of age, smooth pursuit responses improve and are more related to target velocity.

The initiation of smooth pursuit may show larger eye accelerations for vertical pursuit than for horizontal pursuit (the opposite of the case for predictable pursuit, as discussed in the next section); this difference may be evident during diagonal tracking (Fig. 4–4). In the horizontal plane, pursuit accelerations are higher when the target moves towards the midline. In the vertical plane, responses are greater during stimulation of the inferior visual hemifield, irrespective of the direction of target movement. Smooth-pursuit responses do not appear to correspond to the perceptions of target motion, which are stronger along the horizontal or vertical meridian than diagonally. Initial acceleration is unaffected by whether the eye starts in a central or eccentric position. If the target motion is towards the subject, and the trajectory is aligned with one eye, disjunctive smooth-pursuit movements are generated; these are discussed further in Chapter 8.

The early phase of the response also shows damped pursuit oscillations—so-called “ringing”—at a frequency of 3 Hz–4 Hz and, often, an initial velocity overshoot of the target (Fig. 4–3); these findings are present in both the horizontal and vertical planes (Fig. 4–4). Velocity overshoot and “ringing” during pursuit onset, however, are not present in every subject and are influenced by test conditions such as change in luminance of the target and background at stimulus onset. Moreover, the offset of smooth pursuit in response to cessation of target motion (Fig. 4–3) is usually different from the onset: after a latency slightly smaller than the onset, eye velocity declines exponentially to zero with a time constant of about 90 ms. As discussed above, the lack of any sustained “ringing” during cessation of pursuit has been used as evidence that visual fixation is due to a different mechanism than smooth pursuit. However, in some reports such ringing at the time of pursuit onset might be caused by sudden change in luminance corresponding with presentation of the pursuit target. The onset of smooth pursuit is an open-loop, pre-programmed response; Learning is possible, similar to that of saccades; this is a form of pursuit adaptation, which is discussed in a following section.

Smooth Pursuit Responses during Sustained Tracking

Two types of stimuli are commonly used to test smooth pursuit: sine wave and constant velocity movements (ramps or saw-tooth wave-
forms). In addition, “pseudorandom” stimulus motion is sometimes used.

During smooth pursuit of a sinusoidal target motion, performance conventionally is evaluated by measuring gain (peak eye velocity/peak target velocity) and phase. Phase is a measure of the temporal synchrony between the target and the eye. During ideal pursuit tracking, the gain is close to 1.0 and the eye does not lag behind the target (i.e., phase shift is small). Breakdown in smooth pursuit of a sinusoidal stimulus is indicated by a decrease in gain and by the appearance of a phase lag of the eye with respect to the target at higher frequencies. Although gain and phase may be plotted as functions of frequency (as a Bode plot—see Fig. 2–6C), deterioration of smooth pursuit may also be related to increasing target acceleration.\(^{288,384}\) Usually, target amplitude is kept constant so that an increase in target frequency is also accompanied by an increase in peak acceleration and in peak velocity. If, on the other hand, stimulus frequency is held constant, pursuit also declines if the amplitude of the target motion increases. A demonstration of this is shown in Figure 4–5A. The subject is able to pursue a target moving at a frequency of 1.0 Hz if its amplitude is small (5 degrees, peak-to-peak). If the frequency of the target movement is held at 1.0 Hz but its amplitude is increased, smooth pursuit deteriorates. Evidence to show that such deterioration is not due to target velocity is provided by the observation that, with constant-velocity targets (ramps), pursuit gain does not significantly deteriorate until target velocity exceeds about 100 degrees per second (Fig. 4–5B).\(^{315}\) Up to this velocity saturation, gain is typically less

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**Figure 4–4.** Comparison of horizontal and vertical components of the smooth-pursuit response to a diagonal (45-degree direction) step-ramp stimulus. Note that the velocity of the vertical eye component increases faster (higher acceleration of smooth pursuit initiation), although the horizontal component has a greater maximal velocity. Also note that both horizontal and vertical velocity components overshoot the target velocity and show transient oscillations. Positive values correspond to rightward and upward movements. (Rottach KG, Zivotofsky AZ, Das VE, Averbuch-Heller L, DiScenna AO, Poonyathalang A, Leigh RJ. Comparison of horizontal, vertical and diagonal smooth pursuit eye movements in normal human subjects. Vision Res 36, 2189–2195, 1996, with permission from Elsevier.)
than 1.0, but is fairly constant. Therefore, it is important to study pursuit responses with both constant velocity and with sinusoidal target motions. From the responses to constant-velocity stimuli, steady-state pursuit gain and the threshold of the velocity saturation of pursuit can be determined. From responses to sinusoidal stimuli, the acceleration saturation of smooth pursuit to predictable target motion can be determined. By analyzing the responses in this way, a number of characteristic pursuit deficits due to specific disorders have been defined. Examples are shown Figure 4–6 and are discussed in the final section of this chapter.

Generally, smooth pursuit of predictable target motions is superior to that of non-predictable motions such as step-ramps. For example, values of peak eye acceleration in response to predictable sinusoidal stimuli may
exceed 1000 degrees per second per second. \textsuperscript{288} Horizontal smooth pursuit is usually superior to vertical smooth pursuit for sustained responses to predictable target motions;\textsuperscript{18,388} in some subjects, this is the opposite to what is found during the onset of pursuit (Fig. 4–4), suggesting different mechanisms. Downward pursuit may be superior to upward pursuit. \textsuperscript{222a} An important characteristic of the pursuit responses to predictable target motions is their variability. Even normal, young subjects show considerable inter-subject variability. For example, for target motion at a constant velocity of 30 degrees per second, gain ranges from below 0.8 to about 1.0.\textsuperscript{288, 285,391} Some of the variability reflects differences in testing protocols and analysis procedures; thus it is important for each laboratory to determine its normal range of responses. Smooth pursuit gain is reduced if pursuit is performed with the eye in an eccentric position in the orbit; this cannot be ascribed to the effects of orbital mechanics, since pursuit initiation is not similarly affected.\textsuperscript{300} A number of studies have measured the deterioration of smooth pursuit that occurs with age.\textsuperscript{361,402,413,495} The main change is a decrease of the steady-state gain for ramp target stimuli. With sinusoidal stimuli, there is a further decline in gain with high target accelerations (above about 400 degrees per second).\textsuperscript{495} These changes should be kept in mind when evaluating elderly patients. Some technical points about how to make the different pursuit measurements are reviewed below, under Laboratory Evaluation of Fixation and Smooth Pursuit.

Smooth pursuit may also be tested with less predictable “pseudorandom” or “sum-of-sine waves” stimuli.\textsuperscript{24,28,99,491} With such stimuli, pursuit tracking is optimized (minimal phase shift) at some frequency, at the expense of poorer tracking (larger phase shifts) at lower frequencies. Similar results have been reported for optokinetic responses.\textsuperscript{482}

\section*{ADAPTIVE PROPERTIES OF SMOOTH PURSUIT}

The brain uses vision to monitor the performance of smooth-pursuit eye movements. At one
level, this amounts to a negative feedback control (an issue discussed further in the section on Models of Smooth Pursuit). Thus, with ability to adjust performance on a moment-by-moment basis, it may not seem necessary to have evolved an ability to plastically adapt the properties of the smooth-pursuit system. Adaptive properties are well developed for the vestibulo-ocular reflex, which is open loop; vestibular eye movements do not affect the motion-sensing organs in the ear.

Early suggestions of adaptive properties of smooth pursuit were reported from a patient with right abducens nerve palsy, who preferred to view with his paretic eye. It was noted that smooth pursuit by the normal left eye appeared to be too fast (see Fig. 4–7 and Video Display: Disorders of Smooth Pursuit). One specific reason to be able to adapt the performance of pursuit movements to current visual demands arises from the long latency to onset of these movements (about 100 ms). There is a need to generate pursuit movements based on prior experience. Much work on adaptive properties of smooth pursuit has focused on initial responses to step-ramp stimuli. Thus, if the target first steps away from center position and then ramps in the opposite direction, a sudden 90-degree change in the direction of target motion as it crosses midline can induce adaptive pursuit responses within 30 minutes of training.

If target speed is altered during the duration of catch-up saccades, adaptive changes occur in both pre- and post-saccadic eye speed; such changes are direction-specific, but generalize to target motions in different parts of the visual field than those used for training. The contextual relevance of the cue is also important in governing pursuit adaptation; thus targets presented in specific fields of gaze are more likely to induce adaptive changes (since they may be called upon if there is an ocular motor paresis) than the color of the target. There is also evidence that changes in motion perception occur during adaptation of smooth pursuit, and that extraretinal signals are used in achieving adaptation.

What is the neurobiological substrate for smooth-pursuit adaptation? Stimulation of neurons in the middle temporal (MT) visual area to coincide with pursuit responses can induce adaptive changes in the responses. When subjects track asymmetric target motion (ramps upward with resetting steps downward), they develop downbeat nystagmus, a disorder often caused by disease affecting the flocculus. The pathogenesis of downbeat nystagmus is discussed further in Chapter 10. Adaptation of the vestibulo-ocular reflex leads to changes in smooth pursuit, suggesting a shared mechanism underlying both systems, to which the cerebellar flocculus probably contributes. The contextual relevance of the cue is also important in governing pursuit adaptation; thus targets presented in specific fields of gaze are more likely to induce adaptive changes (since they may be called upon if there is an ocular motor paresis) than the color of the target. There is also evidence that changes in motion perception occur during adaptation of smooth pursuit, and that extraretinal signals are used in achieving adaptation.

NEURAL SUBSTRATE FOR SMOOTH PURSUIT

Here we present a hypothetical scheme for the generation of smooth-pursuit eye movements based on prior experience. Much work on adaptive properties of smooth pursuit has focused on initial responses to step-ramp stimuli. Thus, if the target first steps away from center position and then ramps in the opposite direction, a sudden 90-degree change in the direction of target motion as it crosses midline can induce adaptive pursuit responses within 30 minutes of training. If target speed is altered during the duration of catch-up saccades, adaptive changes occur in both pre- and post-saccadic eye speed; such changes are direction-specific, but generalize to target motions in different parts of the visual field than those used for training. The contextual relevance of the cue is also important in governing pursuit adaptation; thus targets presented in specific fields of gaze are more likely to induce adaptive changes (since they may be called upon if there is an ocular motor paresis) than the color of the target. There is also evidence that changes in motion perception occur during adaptation of smooth pursuit, and that extraretinal signals are used in achieving adaptation.

What is the neurobiological substrate for smooth-pursuit adaptation? Stimulation of neurons in the middle temporal (MT) visual area to coincide with pursuit responses can induce adaptive changes in the responses. When subjects track asymmetric target motion (ramps upward with resetting steps downward), they develop downbeat nystagmus, a disorder often caused by disease affecting the flocculus. The pathogenesis of downbeat nystagmus is discussed further in Chapter 10. Adaptation of the vestibulo-ocular reflex leads to changes in smooth pursuit, suggesting a shared mechanism underlying both systems, to which the cerebellar flocculus probably contributes. In addition, the dorsal cerebellar vermis has been shown to be important for adaptive control of the initial 100 ms—the open-loop response—of pursuit tracking.

NEURAL SUBSTRATE FOR SMOOTH PURSUIT

Here we present a hypothetical scheme for the generation of smooth-pursuit eye movements.
using information from both humans and monkeys. As we have stated elsewhere, caution is required in extrapolating results from different species, and in linking behavioral deficits to neuronal activity that is monitored by electrophysiological measures or functional imaging.

Thus, the scheme summarized in Figure 4–8 and Figure 6–7 remains hypothetical.

There is general agreement that there are two functional divisions of the visual system, although there is some debate about how they should be defined.\textsuperscript{32,120,222,294,459,465} Thus, one
scheme, which is primarily based in anatomy, equates vision of moving stimuli with retinal ganglion cells that project via the magnocellular layers of the lateral geniculate nucleus to layer 4C of primary visual (striate) cortex. A second anatomical scheme is primarily concerned with feature analysis (e.g., color) and projects via parvocellular layers of the lateral geniculate nucleus to layer 4C of primary visual cortex. The latency of neurons in layer 4C to flashing spots of light is about 20 ms longer than those in layer 4C.

Chemical lesions of the magnocellular pathway in the lateral geniculate nucleus impair but do not abolish smooth pursuit.

As mentioned above, a second division is based upon psychophysical and ocular following responses to first-order motion stimuli, which are luminance-defined versus second-order motion stimuli, which depend on higher-level mechanisms such as contrast and flicker.

At present, the contributions of different cortical areas to processing of first-order and second-order motion stimuli are still being elucidated.

Primary Visual Cortex and Smooth Pursuit

Primary visual cortex (V1, Brodmann area 17, striate cortex) contains neurons that respond to moving visual stimuli. Such “complex” cells, however, have small visual fields and a narrow range of preferred target speeds. Neurons in V1 respond to first-order, but not second-order, motion stimuli. Using step-ramp stimuli, it has been shown that unilateral lesions of striate cortex abolish smooth pursuit of targets moving in the defective hemifield, contralateral to the side of the lesion, but pursuit remains intact for stimuli moving in any direction that are presented into the normal hemifield. During tracking of predictable target motion, smooth pursuit is usually normal due to the predictable properties of smooth pursuit and the sparing of the macular projection.

Contributions of the Middle Temporal Visual Area

ANATOMICAL CONSIDERATIONS

Striate cortex projects to the middle temporal visual area (MT or V5) that, in rhesus monkey, lies in the superior temporal sulcus (see Fig. 6–8). The projections from striate cortex to MT depend on arcuate, subcortical fiber bundles; there is a direct pathway and an indirect pathway via peristriate cortex. The projections from striate cortex to MT are retinotopic and entirely ipsilateral. Most neurons in MT encode the speed, acceleration, and direction of moving visual stimuli; preferred stimulus velocity is typically 30 degrees per second.

Some neurons in MT have larger receptive fields than those in striate cortex. Neurons in MT show responses to second-order motion stimuli, such as stationary flashed targets, but generally show stronger responses to first-order stimuli.

PHYSIOLOGICAL PROPERTIES OF NEURONS IN MIDDLE TEMPORAL AREA

If complex visual stimuli such as two-dimensional plaids are presented, some neurons respond not to the direction of either component, but rather to the resultant global direction of the stimulus. Similarly, in response to two small targets, which move in different directions, some MT neurons initially encode the vector average of the two motions; however, after about 450 ms, such neurons encode the direction of motion of the target that has been selected for smooth pursuit (winner-take-all). Further insights have also been gained by presenting a set of moving dots that lie within a patch, which moves in a different direction than the component dots. Initially responses of MT neurons are to the local motion of the dots but eventually shift to respond to the global motion of the patch. These neural responses are somewhat similar to the behavioral responses of humans who track line-figure diamonds; initially the eye movement is a vector average of the diamond's line segments, but the response eventually becomes tracking of the motion of the object. Microstimulation in MT during tracking of a smoothly moving target increases smooth pursuit eye velocity, and may induce smooth eye movements even if the target is stationary. Furthermore, MT stimulation that coincides with smooth tracking responses can induce pursuit adaptation. Finally, there is evidence that neurons in MT contribute not only to behavioral responses, but also to speed perception.
THE HUMAN HOMOLOGUE OF MIDDLE TEMPORAL AREA

Based on functional imaging studies, the probable homologue of MT in humans is located posterior to the superior temporal sulcus, at the junction of Brodmann areas 19, 37, and 39, close to the intersection of the ascending limb of the inferior temporal sulcus and the lateral occipital sulcus (see Fig. 6–7, Chapter 6). Different regions of human MT may be activated during smooth pursuit, optic flow, or non-visual pursuit.

EXPERIMENTAL AND HUMAN LESIONS OF MIDDLE TEMPORAL AREA

In monkeys, discrete chemical lesions of those portions of MT that encode visual inputs from the extrafoveal (peripheral) visual field cause a scotoma for motion, and these animals cannot estimate the speed of a moving target. Normally, not only pursuit but also saccades are programmed to take into account the speed of target motion. After MT lesions, the initiation of smooth pursuit is decreased, and the saccades to moving targets are dysmetric for stimuli presented in the affected portion of the visual field. In contrast, saccades made to targets that are stationary within the affected field are normal. Thus, the deficit caused by a lesion of extrafoveal MT is one of visual processing of moving stimuli, rather than of pursuit per se. Moreover, this visual defect is accompanied by a selective loss of motion perception.

Patients with selective lesions at the presumed human homologue of MT have defects of motion perception (akinetopsia) and impairment of smooth pursuit, similar to those described in monkeys with MT lesions (Fig. 4–9).

Contributions of the Medial Superior Temporal Visual Area

ANATOMICAL CONSIDERATIONS

Area MT in rhesus monkey projects to the medial superior temporal visual area (MST), which lies adjacent to MT in the superior temporal sulcus (see Fig. 6–8). In addition, area MT projects via the major forceps and splenium of the corpus callosum to areas MT and MST of the contralateral hemisphere. In rhesus monkey, area MST lies in the superior temporal sulcus (STS), and has two important divisions: a ventrolateral portion (MSTl) and a dorsal region (MSTd).

PHYSIOLOGICAL PROPERTIES OF NEURONS IN VENTROLATERAL PORTION

The neurons in MSTl respond best to motion of small spots of light and seem concerned with smooth pursuit. Their responses are also influenced by visual stimuli presented in the region surrounding their receptive field. Neurons in MST differ from those in area MT by taking into account the effects of eye movements. Such neurons also discharge during anticipatory pursuit movements or pursuit to imaginary target motion. Thus, it seems likely that an efference copy of the eye movement command is sent to these neurons perhaps via thalamic nuclei. Human studies suggest that an efference copy of smooth pursuit movements is used in planning saccades, especially if visual cues are absent. MST neurons also receive a vestibular signal; thus, during eye-head tracking, some MST neurons also encode target motion in world-centered coordinates. It seems that MST plays an important role during smooth pursuit of a small target across a textured background, or fixation of a stationary target during self-motion. This summation of a visual signal and an efference copy of eye movement is similar to that proposed in certain models of smooth pursuit. Because these MST neurons combine visual and eye movement signals, they may encode the motion of the moving visual stimulus in a craniotopic (head-centered) rather than a retinotopic (eye-centered) frame of reference. Indeed, to understand the contributions of visual areas MT and MST to motion vision and smooth pursuit, it is necessary to consider how the population of neurons code responses to motion stimuli.

PHYSIOLOGICAL PROPERTIES OF NEURONS IN DORSAL REGION

The neurons in MSTd seem particularly suited to analysis of optic flow and the direction of heading. They have large receptive fields,
and respond at short latencies to rotations and expansions of visual stimuli, and to speed gradients across the visual field.\textsuperscript{130,227} The response of individual neurons in MSTd to moving stimuli is influenced by the disparity between the locations of images of the same target on the two retinas;\textsuperscript{390} such motion disparity information provides information about self-motion and the layout of the environment. Vergence angle also influences their responses,\textsuperscript{211} and some units respond to smooth vergence tracking.\textsuperscript{6} Further, MSTd neurons receive vestibular inputs,\textsuperscript{359} sense the direction of heading,\textsuperscript{132} and seem able to contribute to spatial orientation, based on motion parallax information.\textsuperscript{133} Like MT neurons, the activity of those in MST can be linked to perceptions of motion.\textsuperscript{8,80,422}

Availability of an eye movement signal is important if the direction of heading is to be estimated while the eyes pursue a moving target.\textsuperscript{60} In addition, a neural signal encoding head movement reaches some MST neurons.\textsuperscript{446} Eye and head movement signals would seem to be important to enable smooth pursuit of a small target moving across a textured background while the subject is moving the head or walking. Certain neurons in MST respond to large-field stimuli moving in the opposite direction to that preferred by these same neurons during pursuit of small targets.\textsuperscript{244}

### The Human Homologue of Medial Superior Temporal Visual Area

The human homologues of MT and MST probably lie adjacent, at the occipital-temporal-parietal junction. Thus, when subjects smoothly pursue a small target, there is activation of the lateral occipital-temporal cortex, an area close to the homologue of MT.\textsuperscript{34} However, there is no activation in this area when subjects view a large moving stimulus with the eyes still; this finding implies that extraretinal signals—possibly related to eye movements—are reaching this area, which might be the human homologue of MST.\textsuperscript{34} When targets are tracked attentively, additional activation occurs in the superior parietal lobule, intraparietal sulcus, precuneus, frontal eye field, and precentral sulcus.\textsuperscript{61,105} When human subjects view visual displays that simulate optic flow, functional imaging detects increased activity in the region of the right superior parietal lobe and dorsal cuneus (the probable homologue of V3 in monkey), and bilaterally on the ventral surface of the brain in the occipital-temporal (fusiform) gyrus.\textsuperscript{87,111} Thus, multiple posterior cortical areas are active during the generation of smooth-pursuit eye movements during natural activities, such as locomotion.
EXPERIMENTAL AND HUMAN LESIONS OF MEDIAL SUPERIOR TEMPORAL VISUAL AREA

Experimental lesions of MSTl in monkey produce a unidirectional deficit of horizontal smooth pursuit for targets moving toward the side of the lesion, irrespective of the visual hemifield into which the stimulus falls. In addition, a retinotopic deficit for motion detection, similar to that with MT lesions, occurs for targets presented in the contralateral visual field. Lesions of the adjacent foveal representation of MT produce a similar deficit.

Consistent with the effects of lesions, activation of MSTl (or foveal MT) by microstimulation during smooth pursuit increases eye velocity during tracking towards the side of stimulation and decreases eye velocity during tracking away from the side of stimulation. During steady fixation, electrical stimulation produces lower eye velocity compared with stimulation during smooth pursuit. Combined experimental lesions of MT and MST produce more permanent deficits.

Unilateral, posterior cerebral lesions in humans that may involve the homologue of MST produce a tracking deficit similar to that in monkey, with impairment of ipsilateral pursuit and a defect of motion processing affecting the contralateral visual hemifield (Fig. 4–11). Bilateral lesions involving MST are reported to cause inability to suppress image motion of the background during smooth-pursuit movements.

Contribution of Posterior Parietal Cortex

In rhesus monkey, both MT and MST project via arcuate fiber bundles to posterior parietal cortex (area 7A), which lies ventral to the intraparietal sulcus (see Fig. 6–8). Bilateral lesions involving MST are reported to cause inability to suppress image motion of the background during smooth-pursuit movements.

Contributions of the Frontal Eye Field

Visual areas MT, MST, and posterior parietal cortex have reciprocal connections with the frontal eye field (FEF; Brodmann area 8) in monkeys (see Fig. 6–8). Within a circumscribed part of the ventral (inferior) FEF, in the arcuate fundus and posterior bank, are a population of neurons that discharge for smooth pursuit, but not for saccades. Microstimulation in this region produces smooth eye movements, usually with an ipsilateral component. Such evoked movements can be elicited even during attempted fixation, but boost the responses of ongoing pursuit, suggesting that FEF controls pursuit gain. Individual neurons increase their activity before and during pursuit in a pre-
ferred direction, and generally increase their discharge rate with eye velocity.\textsuperscript{171,440,441} Typically, the onset of neuronal activity occurs 100 ms after target motion and 8ms–20 ms before the eye starts to move.\textsuperscript{171,440} It has also been demonstrated that some caudal FEF neurons also discharge during pursuit of targets moving in both direction and depth (3-D motion).\textsuperscript{158}

In humans, functional imaging indicates that the part of the FEF concerned with smooth pursuit also lies in the inferior lateral aspect of the FEF,\textsuperscript{362,363} lying deep in the anterior wall of the central sulcus, reaching the fundus or deep posterior wall in some subjects.\textsuperscript{387} Lesions of the FEF in monkeys and humans cause a predominantly ipsidirectional defect of the initiation, steady-state, and predictive aspects of the smooth response.\textsuperscript{297,329} Although the pursuit may be impaired in both directions, optokinetic responses may be preserved.\textsuperscript{228,229} Although the FEF seems important for predictive pursuit,\textsuperscript{157} it does not appear to contribute to adaptive responses to step-ramp stimuli that change speed.\textsuperscript{35}

Contributions of the Supplementary Eye Field

The supplementary eye field (SEF), which lies in the dorsomedial frontal lobe, also receives inputs from MST, the posterior parietal lobe, and the FEF.\textsuperscript{203} The contributions of SEF appear to differ from those due to FEF.\textsuperscript{442} The SEF contains neurons that discharge during smooth pursuit,\textsuperscript{189} but such neurons may also carry a head velocity signal, and discharge during vergence pursuit.\textsuperscript{154} Unlike FEF, pharmacological inactivation of the SEF does not impair smooth pursuit or VOR cancellation during eye-head tracking.\textsuperscript{155} Electrical microstimulation in the SEF increases the velocity of anticipatory pursuit movements and decreases their latency.\textsuperscript{320} This anticipatory pursuit facilitation is greater when stimulation is delivered near the end of the fixation period; no anticipatory smooth eye movements could be evoked during fixation unless there was an expectation of target motion.\textsuperscript{320} Taken together, these reports indicate that the SEF is involved in the process of guiding anticipatory pursuit.\textsuperscript{187,188,191,279,320,449}

Contributions of Other Cortical Areas

In humans, functional imaging indicates that other cortical areas may contribute to smooth pursuit, including the precuneus, anterior, and posterior cingulate cortices.\textsuperscript{49,363} The anterior cingulate and pre-supplementary motor area (pre-SMA) may be important for pursuit responses to predictable target motions.\textsuperscript{393} Further studies may clarify the role that each of these areas plays; indeed, the cerebral contributions to the initiation and maintenance of smooth pursuit are probably due to a distributed network of neurons in several cortical areas. Thus, for example, when subjects attend to a smooth-pursuit target that is intermittently blanked for a second, FEF, SEF, superior parietal lobe and intraparietal sulcus all maintain activation, and may be concerned in sustaining pursuit by using extraretinal signals and working memory.\textsuperscript{292}

Thus, like the control of saccades, the posterior cortical areas seem more concerned with reflexive aspects of pursuit, whereas the frontal areas are important for internally generated and predictive aspects of smooth tracking.

Descending Pursuit Pathways to the Pons

Traditionally, the pursuit pathway has been viewed as a projection from posterior and anterior cortical areas to the cerebellum, via pontine nuclei; the cerebellum, in turn, projects to brainstem premotor areas, such as the vestibular nuclei (Fig. 6–7). Thus, in monkey, visual areas MT and MST project ipsilaterally through the internal sagittal stratum, the retroeccentric portion of the internal capsule, and the cerebral peduncle. The targets of this projection are the dorsolateral and lateral pontine nuclei.\textsuperscript{39,169,453} The projections from MT and MST to the nucleus of the optic tract and accessory optic system are discussed in a separate section below.

In the human brain, the descending pathway is thought to originate in parieto-temporo-occipital cortex; it runs along the lateral surface of the lateral ventricle (internal sagittal stratum), turns medially above the temporal horn, and then toward the posterior limb of the
internal capsule. The FEF pursuit area projects to the caudate nucleus, which has been shown to be important in monkeys who are rewarded for performing specific eye movement tasks. A clinical lesion of the internal sagittal stratum that did not impair smooth pursuit was probably located posterior to the critical part of this pathway. At a more caudal level in the pathway, an ipsilateral pursuit deficit has been reported with lesions affecting the posterior thalamus and adjacent retrolenticular portion of the internal capsule, and with lesions of the dorsal midbrain.

In monkeys, the terminations are scattered throughout several pontine nuclei including the dorsolateral pontine nuclei (DLPN) and the rostral portion of the nucleus reticularis tegmenti pontis (NRTP). Pursuit-related neurons in these nuclei encode a variety of visual and ocular motor signals, including eye velocity. Many neurons modulate their discharge during smooth pursuit of a small target in an otherwise dark room and show directional selectivity, with either ipsilateral or contralateral target motion. Some such neurons continue to discharge if the target light is briefly turned off while pursuit continues; this property implies that a non-visual signal (probably efference copy) encoding eye movement is reaching these neurons; this property is similar to that shown by some MST neurons. Microstimulation in DLPN does not cause smooth eye movements during fixation, but accelerates the eye if the monkey is engaged in smooth pursuit; this result is similar to stimulation in MST. Microstimulation in rostral NRTP produces predominantly upward eye movements.

Discrete chemical lesions of DLPN produce a deficit of smooth pursuit that is predominantly for ipsidirectional target motion. An accompanying saccadic deficit to moving stimuli is directional, unlike the retinotopic defect that occurs following MT lesions. Pharmacological inactivation of DLPN with muscimol impairs initiation of ipsilateral smooth pursuit and steady-state tracking. Pharmacological inactivation of NRTP impairs smooth pursuit onset. The major projections of the pontine nuclei are to the vestibulocerebellar paraflocculus and flocculus, and the dorsal vermis of the cerebellum but, based upon clinical studies the cerebellar hemispheres also contribute to pursuit. One interpretation of these results is that projections from FEF concerned with the onset of smooth pursuit pass via NRTP to the dorsal vermis, whereas projections from MT and MST concerned with maintenance of smooth pursuit pass via DLPN to the flocculus and paraflocculus.

It has been proposed that, similar to the saccadic system, cerebral areas concerned with smooth pursuit also project to ocular motor neurons via the basal ganglia, superior colliculus, and brainstem reticular formation. Thus, the FEF pursuit area projects to the caudate nucleus, which is activated during human smooth pursuit. One target of the caudate nucleus is the substantia nigra, pars reticulata (SNpr), where some neurons cease discharge during pursuit; microstimulation of SNpr during pursuit onset may suppress ipsiversive, and enhance contraversive, pursuit responses. The SNpr exerts important controls on the superior colliculus during programming of saccades (reviewed in Chapter 3); similar mechanisms might operate for smooth pursuit. Thus, in the rostral superior colliculus, neurons modulate their discharge during smooth pursuit in a way that suggests selectivity for stimuli that will be the targets for pursuit and saccades, including gap stimuli (fixation light turned off before target light is turned on).

Although chemical lesions of the paramedian pontine reticular formation (PPRF) were reported to spare smooth pursuit, some pontine neurons have been reported that carry both pursuit and saccadic signals, and may also contribute to the latch circuit for saccades (see Fig. 3–9, Chapter 3). There is also anatomical evidence that pursuit signals from FEF are sent to the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF), which is important for generating vertical saccades. Omnipause neurons, which are known to gate the onset and end of saccades, also decrease their discharge during smooth pursuit.

A hypothetical scheme has been proposed that incorporates a mechanism that gates both smooth-pursuit and saccadic responses, and comprises the rostral pole of the superior colliculus (fixation zone), the omnipause neurons, and the latch neurons in the PPRF. This suggestion will no doubt serve as the impetus to
new experiments, but evidence strongly supports the pathway running from the pontine nuclei to the cerebellum as being critical for normal smooth tracking.

The Cerebellar Contribution

THE VESTIBULOCEREBELLUM AND SMOOTH PURSUIT

A major projection of the pontine nuclei is to the vestibulocerebellum (paraflocculus and ventral flocculus—see Figure 6–6, in Chapter 6).169,339 These structures also receive mossy fiber inputs from the vestibular nucleus, nucleus prepositus hypoglossi, cell groups of the paramedian tracts,72 and climbing fiber inputs from the contralateral inferior olive. The main efferent pathways of the paraflocculus and flocculus are to the ipsilateral superior and medial vestibular nuclei, and the y-group.269 The paraflocculus may also project to the posterior interpositus and dentate nuclei.340 The major anatomical connections are summarized in Box 6–10, in Chapter 6.

It currently appears that the ventral paraflocculus is more important for the control of smooth pursuit, and the flocculus for controlling the vestibulo-ocular reflex.339,373 Purkinje cells in the paraflocculus and flocculus modulate their discharge according to gaze velocity and position during smooth pursuit or passive eye-head tracking (fixation of a head-fixed target during rotation in yaw).235,284,289,290,319 If the monkey fixes a stationary target during passive head rotation, no significant modulation of these neurons occurs, consistent with gaze velocity remaining as zero. However, during active eye-head tracking, the flocculus may play a smaller role.42-44 Some of these floccular neurons modulate their activity with ipsilateral, horizontal pursuit movements; others discharge preferentially for downward movements. Some neurons show transient bursts of activity that might help initiate pursuit.235,260 Microstimulation of the ventral paraflocculus produces smooth eye movements within 10 ms, even during attempted fixation.41 Typically the initial eye movement is upward and contralateral to the side of stimulation. After pursuit adaptation training, Purkinje cells show changes in both simple and complex-spike discharge rates, but it remains an open issue whether these changes reflect learning in the cerebellar cortex or elsewhere.219 Bilateral ablative lesions of the flocculus and paraflocculus greatly impair smooth pursuit.373,486 Unilateral inactivation of the flocculus impairs ipsilateral smooth pursuit43 (see Box 12–2). The deficit following lesions of the flocculus and paraflocculus is a low pursuit gain, differing from that following total cerebellectomy, which totally abolishes smooth pursuit.474,475 This difference confirms that other areas of the cerebellum also contribute to smooth pursuit. Lesion studies suggest that the uvula may influence pursuit responses, although most of its neurons respond to large-field (optokinetic) rather than small moving visual stimuli.190 Two other cerebellar regions also contain neurons that discharge for smooth pursuit: the dorsal vermis and the caudal fastigial nucleus.

THE DORSAL VERMIS AND SMOOTH PURSUIT

Lobules VI and VII of the dorsal vermis also receive inputs from the pontine nuclei, such as NRTP; other inputs are from the paramedian pontine reticular formation (PPRF), vestibular, and prepositus hypoglossi nuclei.455 These anatomical connections are summarized in Box 6–12, in Chapter 6. Purkinje neurons in the dorsal vermis encode gaze velocity during smooth pursuit or combined eye-head tracking.408,425,429 However, they differ from Purkinje cells in the vestibulocerebellum by also responding to retinal slip velocity during deficient pursuit or fixation. Thus, vermal Purkinje cells encode the sum of gaze velocity and retinal image velocity: target velocity in space.223,431 Microstimulation evokes changes in smooth eye movement only during pursuit, not during fixation.264 In humans, transcranial magnetic stimulation over the posterior cerebellum accelerates ipsilateral smooth pursuit.349 Experimental lesions of the dorsal vermis impair the onset of smooth pursuit, reducing initial acceleration by over 50%. In contrast, maintenance of pursuit of a target moving in a triangular waveform was preserved. The ability to adapt pursuit to novel visual demands was also impaired for the initial, open-loop period (see Box 12–4).437 Cerebellar infarction that involves the posterior vermis impairs smooth
pursuit, more so ipsilaterally with unilateral lesions. 458

THE FASTIGIAL NUCLEUS AND SMOOTH PURSUIT

The caudal fastigial nucleus (the fastigial oculomotor region—FOR), which is important in the control of saccades, also contributes to smooth pursuit. 153 It receives inputs from the Purkinje cells of the dorsal vermis and also axon collaterals from pontine nuclei (see Box 6–13, in Chapter 6). 344 Neurons in the caudal fastigial nucleus discharge most vigorously during the acceleration phase of smooth pursuit at its onset; they sustain a lower firing rate during the subsequent, steady-state pursuit movement. 153 Although these neurons modulate their discharge during head movements, they do not encode gaze velocity. Their pattern of discharge at pursuit onset suggests that these neurons may help accelerate the eye during contralateral pursuit. 153 Thus, this pattern is similar to the activity of caudal fastigial nucleus neurons during saccades. 152

Unilateral inactivation with muscimol decreases the acceleration of contralateral pursuit onset and increases the acceleration of ipsilateral pursuit onset; sustained pursuit is impaired in all directions, but most for horizontal, contralateral pursuit (see Box 12–4). 385 This pattern of pursuit asymmetry is similar to that reported in Wallenberg's syndrome (lateral medullary infarction), in which lateral medullary infarction interrupts olivary inputs to the cerebellar cortex, possibly leading to excessive inhibition of one fastigial nucleus. 469 Paradoxically, bilateral fastigial inactivation causes little net effect on eye acceleration during pursuit onset, but impairs sustained pursuit responses in all direction. 385 There is little effect on pursuit latency. Patients with bilateral lesions affecting the fastigial nucleus may appear to show preservation of pursuit, 79 if the onset of tracking is not tested.

Thus, it seems likely that while the dorsal vermis and caudal fastigial nucleus contribute to the onset of smooth pursuit, the vestibulo-cerebellum may be more important during steady-state tracking. Although the projections from the caudal fastigial nucleus to saccade-related structures are known, it is not clear how signals related to smooth pursuit reach ocular motoneurons.

The Accessory Optic System and Nucleus of the Optic Tract

In humans, the pathway that runs from extrastriate areas MT and MST, and the frontal eye fields, to the pontine nuclei and cerebellum appears to play the major role in generating smooth-pursuit eye movements. However, there is another pathway by which visual inputs can lead to smooth eye movements; this is via the accessory optic system (AOS) and the nucleus of the optic tract (NOT), and is summarized in Figure 4–8. 71, 149, 151, 160, 168, 197, 337, 484

The AOS comprises a group of midbrain nuclei that receive mainly contralateral retinal inputs via the accessory optic tract: the dorsal terminal nucleus (DTN), the lateral terminal nucleus (LTN), the medial terminal nucleus (MTN), and the interstitial terminal nucleus (ITN). 337 The retinal afferents to AOS encode retinal slip: neurons in DTN respond to horizontal stimulus motion, and neurons in LTN and MTN respond better to vertical motion. The AOS projects to the dorsal cap of the inferior olive, and the nucleus prepositus hypoglossi–medial vestibular nucleus (NPH-MVN) region. Although neurons in LTN do respond to moving visual fields, their responses saturate above 15 degrees per second. 336 Thus, the AOS may be more concerned with visual adaptation of the vestibulo-ocular reflex than with generation of smooth-pursuit or optokinetic eye movements per se.

The NOT is a pretectal nucleus that lies in the brachium of the superior colliculus, from which it receives its retinal inputs. It projects to the pontine nuclei, including DLPN and NRTP, and the inferior olive, but only weakly to the NPH-MVN region (Fig. 4–8). 71 The NOT also sends substantial projections to the magnocellular layers of the lateral geniculate nucleus, the pregeniculate nucleus, thalamic nuclei (including pulvinar), the mesencephalic reticular formation, and the superior colliculus. Neurons in NOT encode retinal error position, velocity, and acceleration; 108 this information is mainly provided to NOT by projections from MT, MST, and striate cortex. 125, 126, 197 An important aspect of the projections to NOT is that whereas neurons in MST variously show preferences for ipsilateral or contralateral stimulus motion, neurons in NOT respond only to ipsilateral stimuli. 151, 335 This rectification of the output from cortical visual areas has
been shown to depend on crossing, callosal projections of neurons. A similar organization of other cortical areas—such as FEF—may explain why there appears to be no predominance of preferred direction based on neuronal activity, but lesions cause predominantly ipsilateral pursuit deficits. Thus, stimulation in NOT produces nystagmus with ipsilateral slow phases. Most NOT units respond preferentially to movement of a large-field visual stimulus toward the side of recording; they respond to visual stimuli of up to 60 degrees per second. Lesioning the NOT abolishes or impairs smooth pursuit and slow phases of optokinetic nystagmus directed towards the side of the lesion, although some recovery occurs. In sum, NOT appears to play an important role in the generation of eye movements to large, moving visual stimuli, such as the early and late components of optokinetic nystagmus. Since NOT and DTN receive visual inputs from both retina and cortical visual areas, what are the relative contributions of each input to the optokinetic response? Bilateral occipital lobotomies in monkeys impair the optokinetic responses in three ways: the initial high-acceleration, “pursuit” component of the response to a constant velocity stimulus is abolished; the “velocity-storage” component is poor (low and variable gain) for high retinal-slip velocities; monocular optokinetic response is better when the stimulus moves temporal-nasally than nasal-temporally, a nasal-temporal asymmetry. These optokinetic properties are similar to those shown by the normal rabbit. Unilateral hemisphere lesions, such as hemidecortication or localized destruction of area MST cause deficits 1 and 2 above, but not 3. How much does the accessory optic pathway contribute to the optokinetic responses in humans? In newborn babies, in whom pathways to the cerebral visual areas remain immature, optokinetic responses show certain similarities to those obtained in the rabbit; for example, monocular optokinetic responses show temporal-nasal asymmetry. Disappearance of this temporal-nasal asymmetry between 2 and 6 months of life implies that a pathway from retina to NOT and AOS is functioning in humans at birth but that, with the maturation of the cortical visual pathways, projections via extrastriate areas MT and MST to the brainstem supersede. However, when amblyopia or strabismus prevents normal development of binocular vision, nasal-temporal asymmetry of the optokinetic responses persists. When binocular vision does not develop normally, the responses of NOT neurons are affected, and may contribute to the syndrome of latent nystagmus (see Smooth Pursuit, Visual Fixation, and Latent Nystagmus). Patients with bilateral occipital-lobe lesions that cause cortical blindness usually lack optokinetic responses; this is our experience and that reported by others. One patient was reported to show a slow build-up of optokinetic nystagmus in one direction, with full-field stimulation, but there was some sparing of visual cortex when his brain was examined post-mortem. Thus, although the NOT and AOS may contribute to visually induced eye movements, the transcortical pathway for optokinetic nystagmus is most important once binocular visual mechanisms are developed. One reason why the transcortical optokinetic mechanism has come to eclipse the brainstem optokinetic pathway in humans may be the evolution of frontal vision and the consequent changes in optic flow that occur during locomotion. The normally developed cortical contribution to optokinetic nystagmus (OKN) in humans provides a directionally symmetrical monocular response, achieves stabilization of images in one depth plane during movement, and ensures that vergence mechanisms are provided with stable retinal images.

Summary of Pursuit Pathway

Figure 4–8 summarizes important pathways for smooth pursuit. Retinal information on the speed and direction of a moving target is abstracted in visual cortex, especially area MT and MST. Such processing takes into account current eye movements, encodes the direction and speed of complex moving stimuli, and allows for the effects of relative motion of the background during pursuit (including the case of fixating a stationary target during self-motion). These signals are passed on to frontal areas, which may contribute to the initiation and predictive properties of the pursuit response. The extrastriate visual areas and frontal cortex concerned with pursuit project to pontine nuclei, especially the dorsolateral pontine nuclei (DLPN) and nucleus reticularis...
tegmenti pontis (NRTP), which contain cells encoding a mixture of eye movement signals and visual information. The NOT, which receives inputs from MT and MST, may also make an important contribution to pursuit by virtue of its projections to the pontine nuclei. The pontine nuclei project to the cerebellum, with DLPN mainly projecting to paraflocculus and flocculus, and NRTP to the dorsal vermis. The cerebellum plays a critical role in generating signals for pursuit from visual and ocular motor inputs. The dorsal vermis and fastigial nucleus may contribute mainly to the onset of pursuit, whereas the paraflocculus and flocculus mainly sustain the pursuit response. The output of the flocculus and parafloucculus is mainly through the vestibular nuclei and y-group (for vertical responses). Further details of the anatomical pathways involved in smooth pursuit may be found in Figure 6–7 of Chapter 6.

MODELS OF SMOOTH PURSUIT

Quantitative hypotheses—models—have played an important role in advancing our understanding of how the brain programs smooth-pursuit eye movements (See “Linear control systems in the oculomotor system” by David A. Robinson, on the accompanying DVD). Visually mediated eye movements, such as smooth pursuit, have traditionally been described as negative feedback control systems. What does this mean? Let us assume that, to start with, the eye is stationary, and a target of interest starts to move at velocity $T$ (Fig. 4–10A). In this case, the stimulus to pursuit is the velocity of motion, or “slip,” of the visual image of the target as it moves away from the fovea, across the retina. In this case, the “error signal,” which is called retinal error velocity (REV in Fig. 4–10A) is equal to target velocity. Retinal error velocity is the signal used by the pursuit system to generate an eye velocity command, $E_v$. Note that as soon as the eye starts to move, retinal error velocity is no longer equal to target velocity. Now, retinal error velocity is the difference between target velocity and eye velocity. This subtraction of eye velocity (via the visual feedback loop) from target velocity, to produce retinal-error velocity, is represented by the summing junction in Figure 4–10A. This subtraction reflects the physical fact that the retina is attached to the eye. The calculation of retinal error velocity is performed by the visual system based on the rate of image movement across the retina. The retinal error signal is “amplified” by the brain to generate an eye movement that will catch up with the target. This model, therefore, uses negative feedback with a central amplification; it is a simple velocity servo.

Ideally, we would want eye velocity ($E_v$ in Fig. 4–10A) to increase until it matched target velocity ($T_v$) so that the image of the moving target would be held steady on the fovea. However, the model shown in Figure 4–10A would not achieve this, because if the retinal error velocity were reduced to zero, then the stimulus for the eye movement would disappear, and the eye would slow down and fall behind the target. This model could achieve a steady state in which a constant, small retinal error velocity remains in order to sustain tracking. Intuitively, it is apparent that if the internal amplification factor (or open-loop gain, $G_{OL}$) is large, then small amounts of retinal slip will still drive an eye movement. A convenient measure of the overall tracking performance is the overall or closed-loop gain, $G_{CL}$, which is given by the ratio: eye velocity/target velocity. An equation relating $G_{OL}$ and $G_{CL}$ is given in Figure 4–10A. It can be seen that for eye speed to be close to target speed ($G_{CL}$ close to 1.0), the value of $G_{OL}$ must be large.

Negative feedback is widely used in physiologic control systems. It offers certain advantages: a prompt and accurate response to stimuli and a relative insensitivity to changes in internal parameters. Consider, for example, the effects of a decline of the value of the internal amplification factor or “open loop gain” $G_{OL}$. Such a decline might occur with disease. From the equation in Figure 4–10A, a decline of $G_{OL}$ from 9.0 to 4.0 would cause $G_{CL}$ to drop only from 0.9 to 0.8. So, a more than 50 percent reduction of $G_{OL}$ would cause only a small effect on overall smooth pursuit gain. Negative feedback also carries a potential risk: oscillations caused by instability. Instability is more likely if the gain, $G_{OL}$, is high and if there are time delays in the system.

Although the model in Figure 4–10 is an over-simplified representation of smooth pursuit, it does make an interesting prediction. If normal closed-loop gain is close to 1.0 (near-perfect tracking), then $G_{OL}$ must be large. This
prediction can be tested experimentally by using a number of techniques to artificially open the visual feedback loop (i.e., dissociate retinal error velocity from the effects of eye movements that it stimulates). For example, the visual feedback loop is “opened” when one eye is immobilized and a moving stimulus is presented to it. In this case, eye movements can no longer affect the velocity at which images drift across the retina. The response to this open-loop stimulation can be studied by measuring the movements of the other eye, which is mobile but covered (to prevent visual feedback). Ter Braak was among the first to perform this experiment (an English translation of his paper can be found as an appendix in the smooth pursuit and visual fixation chapter).
to the monograph by Collewijn). He used optokinetic stimulation in the rabbit and found that the open-loop gain, $G_{OL}$, was indeed high: the covered eye moved many times faster than the stimulus. Similar results have been reported in monkeys. Patients with a complete unilateral ophthalmoplegia and with preservation of vision provide conditions suitable for measuring the open-loop gain. Similar large values have been found for the open loop gain from these studies, particularly for low stimulus velocities. During chronic exposure to such an open loop situation, plastic adaptive changes, for example in the vestibulo-ocular reflex, are also stimulated.

The feedback loop also can be opened in normal subjects by artificially stabilizing stimuli on the retina using electronic feedback systems. Another method is to use photo-flash after-images that are placed close to the fovea. All these methods suffer from the drawback that, during this “open-loop” condition, the mental state of the subject may considerably influence the results. Because there is a time delay in the pursuit response of approximately 100 ms, another method of studying the “open-loop” pursuit response is to measure the movement of the eye that occurs prior to the response of the visual system to that eye movement. This technique measures the initial eye acceleration using step-ramp stimuli and was discussed in the section Onset of Pursuit. Since feedback tends to protect the closed-loop gain of the system, measuring the open-loop response directly is a more sensitive way of determining if there has been a change in the internal workings of the system.

The model of Figure 4–10A incorporates a time delay, which is about 100 ms, and is largely due to delays in the visual system. This delay has an important potential consequence: if the gain $G_{OL}$ is large (high amplification), this negative feedback system would become unstable, with oscillations. Although damped oscillations (“ringing”) occur during smooth pursuit, their magnitude is small and, overall, tracking is relatively stable, thus implying that a simple negative feedback model does not account for normal behavior. This discrepancy led Young and colleagues to postulate that the stimulus to the pursuit system is not retinal error velocity per se, but an internal representation of the motion of the target in space (Fig. 4–10B). This internal representation of target velocity is obtained by combining retinal error velocity with an eye velocity signal, probably based on monitoring of motor commands (efference copy or corollary discharge). The effect of adding this positive, internal feedback loop is to cancel the outer, negative, visual feedback loop; the effective model is therefore “open-loop”. However, if the efference copy loop did not exactly match the visual feedback loop (a plausible possibility, since the former depends on the performance of neurons, but the latter on physics), then certain features of pursuit onset—such as the oscillations at the beginning of the response (Fig. 4–3) could be explained. This model has been extended further, to account for dynamic aspects of pursuit onset, for the effects of pursuit adaptation such as occurs after extraocular muscle palsies, and for the finding that acceleration of images on the retina also drives smooth pursuit onset. It has been proposed that the pendular form of congenital nystagmus (discussed further in Chapter 10) could arise from the mechanism that causes oscillations at the onset of smooth pursuit. Neuroimimetic models have been proposed for smooth pursuit that attempts to incorporate neural networks that simulate the role of MST and account for predictive behavior.

The model shown in Figure 4–10B has also been modified, in a number of ways, to account for the cessation of smooth pursuit, which may be equivalent to visual fixation. One manifestation of an abnormal fixation mechanism is abnormal drifts, which lead to nystagmus (see A Pathophysiological Approach to the Diagnosis of Nystagmus in Chapter 10). In patients with nystagmus who also have disease affecting the visual pathways, such as demyelination in optic neuritis, prolongation of the delay due to visual feedback beyond 100 ms might be the cause of oscillations (see Video Display: Acquired Pendular Nystagmus and Figure 4–11A). In normal subjects, it is possible to induce spontaneous oculomotor oscillations by experimentally increasing the latency of visual feedback during fixation (Fig. 4–11B). However, the frequency of these induced oscillations is less than 2.5 Hz, which is lower than in most patients who have acquired pendular nystagmus in association with optic nerve demyelination. Furthermore, when this experimental technique is applied to patients with acquired pendular nystagmus, it does not change the characteristics of the nystagmus but, instead, superimposes...
lower-frequency oscillations similar to those
induced in normal subjects (Fig. 4–11C). Thus, disturbance of visual fixation due to
visual delays cannot solely account for the high-frequency oscillations that often charac-
terize acquired pendular nystagmus.

During steady-state smooth pursuit of pre-
dictable target motion (such as a sine wave),
many normal subjects can generate eye move-
ments that match target movement with a gain
of 1.0 and no phase shift. Models such as
those in Figure 4–10 cannot account for this
behavior. The same problem occurs when such
models are used to account for sustained visual
fixation: the dynamic properties are better than
could be accounted for the delays in the sys-
tem, especially that due to visual process-
ing. The conclusion from this
discrepancy between model predictions and
observed behavior is that both sustained
smooth pursuit of a moving target and fixation
of a stationary one require a predictor mecha-
nism. Several such models have been pro-
posed, with different topology and underlying assumptions. These models suggest
experiments that are likely to produce new
insights into how the brain generates visually
mediated eye movements. Finally, for a more
critical and detailed appraisal of models of
smooth pursuit, the reader is referred to David
A. Robinson’s hand-written notes on the
accompanying DVD.

CLINICAL EXAMINATION
OF FIXATION AND
SMOOTH PURSUIT

Examining Fixation

First examine the patient’s eyes while they are
in primary position. This should be performed
as the patient views an object located across
the room, and which requires a visual discrim-
ination, such as an optotype of a visual acuity
chart. (Evaluation of the stability of fixation
during eccentric gaze holding is discussed in
Chapter 5.) Next, occlude one eye and observe
the other eye to see if any abnormalities—par-
ticularly latent nystagmus—develop. Switch
the cover and repeat this procedure for the
other eye.

The most sensitive clinical method to evalu-
ate fixation is with the ophthalmoscope: the
patient fixates with one eye while the examiner
views the optic disc of the other eye. Look for
any drifts, nystagmus, or saccadic intrusions. If
nystagmus is observed, examine one eye with
the ophthalmoscope and transiently occlude
the other, to determine if the nystagmus
increases as fixation is prevented.

In evaluating visual fixation, remember that
gaze is less steady in preschool children, and
may be disrupted by saccadic intrusions in
some normal individuals, particularly the
elderly.
Examining Smooth Pursuit

Ask the patient to track a small target with the head still, such as a pencil tip held a meter or more before the eyes. Initially move the target at a low, uniform speed. Pursuit movements that do not match the target velocity necessitate corrective saccades. If these are catch-up saccades, then the pursuit gain is low. If pursuit gain is too high (for example, due to superimposed slow phases of nystagmus), then back-up saccades are seen (see Video Display: Disorders of Smooth Pursuit). During a series of regular to-and-fro movements of the test object, suddenly stop the target motion at a turnaround point and look for a brief continuation of pursuit; this tests the ability of the patient to use a predictive strategy. (See Appendix A for a summary.)

In evaluating smooth pursuit, recall that these movements depend upon the subject’s ability to direct visual attention and are particularly susceptible to the influence of medications. Moreover, “normal” smooth pursuit depends upon the subject’s age; it is not well developed in young infants and more variable in preschool children than in adults. Smooth pursuit performance progressively deteriorates in old age.

In evaluating smooth pursuit, recall that some normal subjects may show directional asymmetries, usually in the vertical plane and sometimes worse for downward tracking. With these qualifications, it is usually possible, with experience, to determine clinically if pursuit is abnormal or, at least, if it warrants quantitative evaluation.

Certain special techniques are often useful for the clinical evaluation of pursuit. Uncooperative or inattentive patients, small children, or those thought to have hysterical blindness may be tested by slowly rotating a mirror held before their eyes; a mirror that is large and fills most of the visual field is a compelling stimulus for visual tracking. Hand-held optokinetic drums or tapes do not adequately test the optokinetic system but do stimulate pursuit. These are useful tools for demonstrating pursuit asymmetries (e.g., with cerebral hemispheric disease) and “reversed pursuit” seen in some patients with congenital nystagmus (see Video Display: Disorders of Smooth Pursuit). Although the corrective quick phases are most evident at the bedside, it is the direction and nature of the slow phases that should be analyzed. For example, a patient with a right posterior cerebral lesion may show fewer corrective quick phases when the drum is rotated to the right side. This is, in part, because the pursuit gain is lower to the right and, because the eyes deviate more slowly from the central position, fewer quick phases are needed.

In some patients, it will be difficult to test smooth pursuit because of spontaneous nystagmus. Sometimes this nystagmus is less prominent in the primary position or at some null point. In these patients, pursuit function can be inferred by testing cancellation or suppression of the vestibulo-ocular reflex with the eyes held in this orbital position (see Smooth Tracking with Eyes and Head in Chapter 7). Patients often do this best by fixating their thumbnail with an arm outstretched, while they rotate their heads. Those who have muscle weakness can be rotated in a wheelchair while fixating the examiner’s pointer, which rotates with the chair (see Video Display: Disorders of Smooth Pursuit). As with pursuit, the rotation should be gentle at first. With inadequate cancellation, the eyes will be continually taken off target by the slow phase of the vestibulo-ocular reflex and corrective saccades will be made. An asymmetrical deficit may imply a pursuit imbalance; for example, deficient cancellation of the VOR on rotation to the right corresponds to a low pursuit gain to the right. When there is a clear discrepancy between the performance of smooth pursuit and cancellation of the VOR (e.g., poor pursuit but good cancellation), then one should suspect an inadequate or asymmetrical VOR.

LABORATORY EVALUATION OF FIXATION AND SMOOTH PURSUIT

An essential prerequisite for smooth pursuit testing is to maintain the alertness and attention of the subject or patient; recording sessions should be kept as short as possible. The most commonly used stimulus for smooth pursuit is a small, bright spot of light, typically from a Helium-Neon laser, projected onto a dark or featureless screen. The position of the target light is usually controlled by mirror galvanometers that lie in the ray’s path. A correction for the tangent error inherent in projecting the stimulus onto a flat screen is necessary for larger target movements; another
solution is to project the target onto an arc at the center of which the subject sits. An alternative to a projected stimulus is a bright spot on a video screen. This method allows more precise control over the stimulus but the range of movement is usually less than the requisite plus and minus 20 degrees useful for clinical testing. Alternatively, a video image may be projected onto a large screen.

To investigate the onset of smooth pursuit, step-ramp or ramp stimuli of various velocities (typically 5 degrees per second to 30 degrees per second) are used (Fig. 4–3). Several advantages are offered by non-predictable, step-ramp stimuli:

1. The initial response of smooth pursuit can be directly related to the stimulus, since there has not been time for any eye movement to influence the visual stimulus (the response is open-loop).
2. Because visual feedback tends to “compensate” for the system’s inadequacies, it follows that the open-loop response to a step-ramp stimulus is a more sensitive index of dysfunction than the closed-loop response that occurs during maintenance of pursuit.
3. Using step-ramp stimuli, it is possible to stimulate selected portions of the extrafoveal visual field, a useful facility in studying, for example, patients with focal cerebral lesions who may have a retinotopic tracking deficit.

The response to step-ramp stimuli may be analyzed to determine: latency to onset of pursuit; average eye acceleration in first 100 ms (“open-loop” response); peak eye acceleration and the time taken to reach it and the velocity at that time; peak velocity of the first overshoot and the time to reach it; frequency of ringing; and steady-state gain.

The relationship between peak eye acceleration and target velocity is one measure of the initiation of smooth pursuit. In some studies, interactive computer programs have been used to identify valid trials, remove saccades, and average the responses to several trials. Averaging programs, however, may hide some of the dynamic features of the response owing to trial-to-trial variations. Blinks are reported to transiently slow smooth pursuit.

Maintenance of smooth pursuit is usually tested with predictable waveforms such as constant velocity (ramp) and sinusoidal target motion. During smooth pursuit of a constant velocity target, the most useful measurement is gain (eye velocity/target velocity). Eye velocity may be estimated either from maximum smooth eye velocity for each trial, or eye velocity as eye passes through primary position. For constant velocity waveforms, gain should be estimated for each of several trials at the same target velocity; then mean gain can be calculated. This should be done for several different target speeds (e.g., 5 degrees per second–50 degrees per second) and directions. These measurements are most easily accomplished by computer programs. Our experience is that interactive approaches, which allow the investigator to exclude saccades or blinks, are more reliable than automated methods.

For sinusoidal target motions, gain may be estimated from peak eye velocity/peak target velocity. The dependence of gain on peak target acceleration is a useful measure of the pursuit performance (see Models of Smooth Pursuit). Alternatively, using digitized data, it is possible to remove saccades and perform a Fourier transform of target and eye signals and thereby compute gain and phase.

A variety of indirect methods are commonly used to measure smooth pursuit performance. Attempts to quantify smooth pursuit by measuring frequency and number of saccades are prone to error, since saccadic abnormalities (e.g., square-wave jerks) may disrupt overall tracking but not necessarily imply impaired pursuit (i.e., pursuit gain may be normal). Similarly, power spectral measurements (e.g., natural logarithm of ratio of the power at target frequency to power at higher frequencies) or root-mean-square error are estimates of overall tracking, not just smooth pursuit. Finally, quantitative rating scales of pursuit as relatively “normal” or “deviant” are of little value in determining the nature of the deficit. (For quantitative aspects of smooth eye-head tracking, see the Evaluation of Eye-Head Movements, Chapter 7.)

ABNORMALITIES OF VISUAL FIXATION AND SMOOTH PURSUIT

Here we discuss the pathophysiology of abnormal visual fixation, abnormal pursuit initiation, abnormalities of pursuit to sustained target motion, and the relationship of visual fixation and smooth pursuit to latent nystagmus and infantile nystagmus syndrome (congenital nys-
tagmus). In Chapters 10–12, these abnormalities are approached from the viewpoint of topological diagnosis.

Abnormalities of Visual Fixation

Steady fixation may be disrupted by slow drifts, nystagmus, or involuntary saccades. Since normal subjects show “miniature” movements of all three types (Fig. 4–1), determination of abnormal fixation behavior sometimes depends on statistical analysis of measured eye movements. One specific example of the problem of determining what is abnormal concerns square-wave jerks (see Fig. 10–15A and Video Display: Saccadic Oscillations and Intrusions). These are small, horizontal saccades (typically 0.5 deg–5.0 deg) that take the eye away from the fixation point and, after a period of about 200 ms, return it to the starting position. Many normal subjects show square-wave jerks when they attempt steady fixation. During attempted fixation of the remembered location of a target, the frequency of square-wave jerks decreases, perhaps because of increased task demands, since there is also a decrease in their frequency during pursuit of faster targets, which requires greater attention. The frequency of these saccadic intrusions increases with age and, in some elderly subjects, is as great as that occurring in certain neurological conditions, notably progressive supranuclear palsy, Friedreich’s ataxia, and focal cerebral lesions. Thus, disruption of fixation by square-wave jerks is only suggestive of an underlying neurological condition; they are discussed further in the section on Saccadic Intrusions in Chapter 10.

The presence of nystagmus during attempted visual fixation of a stationary target is abnormal. If the slow-phase velocity or intensity of such nystagmus is similar both during fixation and when fixation is prevented (e.g., by Frenzel goggles or in darkness), a disorder of the fixation system is inferred. If slow-phase velocity is reduced during attempted fixation, the fixation system is at least partially functioning and another ocular motor disorder (e.g., imbalance of vestibular drives) is present. A variety of conditions may lead to nystagmus during attempted fixation and are discussed in Chapter 10.

Disorders of the visual system lead to instability of gaze; an extreme example is blindness (see Fig. 10–8A of Chapter 10 and Video Display: Nystagmus and Visual Disorders). This nystagmus characteristically changes direction over the course of seconds and minutes (Fig. 10–8A), a feature also encountered following experimental cerebellectomy. Thus, the nystagmus that follows bilateral visual loss reflects a gaze-holding mechanism that has never been calibrated by visual inputs. Acquired lesions of the cerebellum without specific involvement of the visual pathways may disrupt fixation with saccadic intrusions and with slow drifts, especially in the vertical plane, that lead to nystagmus. These abnormalities reflect the important role of the cerebellum in optimizing fixation to provide clearest vision.

Monocular loss of vision may lead to unstable gaze in the affected eye, predominantly due to slow, low-frequency vertical drifts. These movements may reflect disturbance of a monocular fixation system or, perhaps, vertical vergence, which, unlike horizontal vergence, only shows first-order responses to motion stimuli (see Chapter 8).

As discussed in the section on Models of Smooth Pursuit, the pathogenesis of pendular oscillations in association with visual loss is undetermined. Experimental deprivation of information on retinal slip velocity during development causes a 4-Hz to 5-Hz pendular nystagmus, a finding that may be pertinent to congenital forms of nystagmus, which are discussed below. When pendular nystagmus occurs in association with optic nerve demyelination due to multiple sclerosis, the size of the oscillations tends to be greatest in the eye with worse vision. However, experimental studies (Fig. 4–11) indicate that visual delays cannot be the sole cause of their nystagmus.

Abnormalities of Smooth Pursuit

ABNORMALITIES OF PURSUIT INITIATION

The advantages of studying the onset of pursuit are discussed above; in the case of cortical lesions, step-ramp stimuli are particularly valuable because they provide a method of controlling the location of the visual stimulus on
the retina (i.e., in the visual field). Because of the latency of the pursuit system, the initial 100 ms of the response will reflect stimulation of the selected portion of the visual field and can be used to test the effects of lesions affecting the cerebral hemispheres. Thus, using step-ramp stimuli, it has been shown that experimental, unilateral lesions of striate cortex cause a loss of smooth pursuit for targets moving in the blind visual field; this deficit is not evident during pursuit of a predictably moving target partly because of preserved macular vision. In humans, bilateral occipital lobe lesions abolish or prevent the development of smooth pursuit.

More important, it has been possible to identify distinct disturbances of ocular tracking due to lesions of secondary visual areas. One such disturbance was exemplified by a patient who complained of difficulties in seeing moving, but not stationary, objects in his right visual hemifield, following a stroke (Fig. 4–9). Routine perimetric testing of his visual fields was normal. Furthermore, testing of pursuit with predictable, sinusoidal stimuli showed little abnormality. Nevertheless, with step-ramp stimuli, his ocular motor deficits reflected a loss of the ability to estimate the speed of moving objects in the right visual hemifield. Specifically, the initiation of pursuit and planning of saccades to targets moving to right or left, within the right visual hemifield, were impaired. In contrast, saccades made to static target displacements were normal (Fig. 4–9). Thus, these deficits are similar to those described in monkeys after lesions of the middle temporal visual area (MT or V5): a retinotopic defect for the perception of motion. The lesion lay at the junction of temporoparietal cortex (Fig. 4–9), consistent with subsequent functional imaging studies that localized the human homologue of MT to this region.

A second, more common type of tracking deficit occurring with unilateral cerebral lesions consists of a directional pursuit deficit in which horizontal pursuit directed towards the side of the lesion is impaired compared with contralateral pursuit (Fig. 4–12B). Using step-ramp stimuli and measuring the onset of smooth pursuit, it has been demonstrated that this unidirectional deficit occurs irrespective of the visual hemifield into which the stimulus falls (Fig. 4–12C). A retinotopic deficit such as that occurring with lesions of MT may or may not coexist. The unidirectional deficit may occur with lesions affecting posterior cortical areas and underlying white matter (Fig. 4–12A); this may be due to damage to the medial superior temporal visual area (MST) or its projections. In addition, a unidirectional deficit of smooth pursuit may occur following lesions of the frontal lobes that affect the frontal eye field, or the supplementary eye field.

In the future, better understanding of the disturbances of smooth ocular following due to lesions of the cerebral hemispheres may be made possible by presenting first-order and second-order stimuli. The effects of these stimuli on smooth pursuit can be evaluated using a variety of paradigms, including step-ramp and sinusoidal stimuli. Additionally, the use of functional imaging techniques such as fMRI and PET can help to localize the regions of the brain that are involved in the generation and control of smooth pursuit movements.
Figure 4–12. (Continued) (B) An example of asymmetric smooth pursuit in a patient with a porencephalic cyst of the right cerebral hemisphere. Note how smooth pursuit to the right (upward) is impaired, but corrective saccades are accurate. During tracking to the left, eye velocity exceeds target velocity, and "back-up" saccades are made. (C) Step-ramp responses to same patient as in (B). Pursuit initiation in response to rightward ramps is impaired compared to leftward ramps, regardless of the visual hemifield stimulated. In addition to this unidirectional pursuit deficit, saccades made to targets in the left visual hemifield are hypometric or delayed, suggesting a defect of motion processing in that hemifield. Thus this deficit is similar to that described after experimental lesions of the medial superior temporal visual area (MST) or the descending pursuit pathway in monkey.438 R: right; L: left.
ABNORMALITIES OF PURSUIT TO SUSTAINED TARGET MOTION

Low gain pursuit is a common ocular motor abnormality. Attempts have been made to differentiate between a low steady-state pursuit gain in response to constant velocity target motions (i.e., reduced gain at both low and high target velocities—velocity saturation) and a reduction of pursuit gain with accelerating targets (e.g., sine waves)—so-called acceleration saturation. Low steady-state pursuit gain occurs with a variety of conditions, including old age, Parkinson’s disease, progressive supranuclear palsy, cerebellar disorders, hepatic encephalopathy, and following large cerebral lesions (see Video Display: Disorders of Smooth Pursuit). Impairment of smooth pursuit due to an abnormal acceleration saturation is seen with posterior cortical lesions, Alzheimer’s disease, and schizophrenia. Studies of the effects of predictive aspects of smooth pursuit have shown impairment in schizophrenia. Several mechanisms have been proposed, including impaired motion perception, extra-retinal factors, but tracking may also be impaired because of saccadic mechanisms, which appear to constitute an independent problem. In contrast, predictive aspects of pursuit are preserved in patients with Alzheimer’s disease, Parkinson’s disease, who otherwise show poor tracking. Large lesions of the cerebral hemispheres causing predominantly ipsilateral tracking deficits have been reported to impair but not abolish, predictive aspects of smooth pursuit. Frontal lesions may impair predictive smooth pursuit more than posterior lesions. Smooth anticipatory eye drifts that precede predictable target stepping are absent in patients with cerebellar disease who have impaired smooth pursuit. Excessively high tracking gain may reflect pursuit adaptation in response to extraocular muscle palsy (see Video Display: Disorders of Smooth Pursuit, and Fig. 4–7). For example, a patient with right abducens palsy viewed from that eye for several days, his normal left eye being patched. Smooth pursuit responses of his normal left eye were then tested using step-ramp stimuli. Eye velocity to the right was greater than that of the target (Fig. 4–7B) and tracking was unstable with pendular oscillations. These findings imply that pursuit adaptation, rather than simple negative feedback, is used to optimize smooth-tracking performance.

An asymmetry of sustained horizontal smooth pursuit is seen with certain lesions affecting cerebral cortex (see Video Display: Disorders of Smooth Pursuit, and Fig. 4–12B). Thus, some patients with unilateral lesions of the cerebral hemispheres show impaired tracking of targets moving towards the side of the lesion. This has been most commonly reported with lesions restricted to posterior cortical areas and underlying white matter (Fig. 4–12A), but also occurs with frontal lobes lesions, and is variable with large lesions such as hemidecortication. Clinically, this pursuit deficit can often be brought out with hand-held “optokinetic” drums or tapes. This impairment of smooth
pursuit is independent of homonymous hemianopia or visual neglect, but this requires application of step-ramp stimuli, which control the position of the stimulus in the visual field (Fig. 4–12C). In occasional patients with unilateral lesions of the cerebral hemispheres, pursuit away from the side of the lesion may also have reduced gain, though not usually so much as ipsilaterally. In other patients, particularly those with large lesions such as hemidecortication or involvement of the posterior internal capsule, pursuit eye movements away from the side of the lesion may be faster than the target (i.e., smooth pursuit gain exceeds 1.0). An example is shown in Figure 4–12B. One consequence of such increased gain for contralateral pursuit is that the moving target is held in the visual hemifield ipsilateral to the side of the lesion, where the ability to estimate target speed is likely to be normal. Responses to moving stimuli presented into the visual hemifield contralateral to the side of the lesion may be impaired. After an acute large hemispheric lesion, there may be a pursuit defect in craniotopic coordinates, with difficulty moving the eyes in the contralateral orbital hemirange. Especially with right-sided lesions, there may also be contralateral neglect. However, within the remaining field of movement, responses to stimulus motion towards the intact hemisphere are greater.

An ipsilateral pursuit deficit similar to that due to hemispheric disease may be encountered with unilateral lesions at lower points in the descending pursuit pathway (Fig. 4–8) such as in the thalamus, midbrain tegmentum, dorsolateral pontine nucleus, and cerebellum. However, because of the “double decussation” of the smooth-pursuit pathway (see Fig. 6–7), lesions involving the vestibular nucleus or pontine projections to the cerebellum may cause a greater impairment of either ipsilateral or contralateral smooth pursuit. Disturbance of vertical smooth pursuit occurs with bilateral internuclear ophthalmoplegia (INO). Lesions affecting the superior cerebellar peduncle, which conveys pursuit signals from the y-group nucleus to the oculomotor nucleus, may also impair smooth pursuit. An unusual directional disturbance of smooth pursuit has been reported in three patients with cavernous angiomas involving the middle cerebellar peduncle. They all showed torsional nystagmus during vertical pursuit (see Video Display: Disorders of Smooth Pursuit). This finding suggests that pursuit signals might be encoded in the same planes as the labyrinthine semicircular canals, perhaps during cerebellar processing. Lesions restricted to either the paramedian pontine or mesencephalic reticular formation impair saccades but tend to spare horizontal and vertical smooth pursuit.

In some patients with asymmetry of pursuit, nystagmus is present during fixation with the eyes near to primary position. Thus, horizontal nystagmus is reported in some patients with unilateral cerebral lesions, particularly those with increased gain of contralateral pursuit. This nystagmus is low-amplitude, with slow phases drifting away from the side of the lesion at a few degrees per second. Such nystagmus has been hypothesized to indicate an imbalance of pursuit tone. Another circumstance in which an imbalance of pursuit drives has been postulated as a cause of nystagmus concerns downbeat nystagmus. As discussed in Chapter 10, several distinct hypotheses have been proposed to explain this form of nystagmus, but the “pursuit imbalance hypothesis” remains a possible mechanism, since it has been recently shown that normal subjects develop downbeat nystagmus after carrying out repetitive, asymmetric vertical smooth pursuit. Finally, smooth-pursuit performance is sometimes improved in patients with loss of vestibular function. This is presumably an adaptation so that smooth-pursuit eye movements can be used to partially compensate for the vestibular loss. This issue is discussed further in Chapters 2 and 11.

Smooth Pursuit, Visual Fixation, and Latent Nystagmus

Individuals with latent nystagmus, congenital form of nystagmus (see Video Display: Congenital Forms of Nystagmus), show abnormalities of smooth pursuit during monocular viewing. Latent nystagmus is brought out or exaggerated by covering one eye (hence, “latent” nystagmus (see Video Display: Congenital Forms of Nystagmus and Fig. 10–12)). The quick phases of both eyes beat
away from the covered eye. Latent nystagmus is almost always associated with strabismus and lack of development of normal binocular vision and stereopsis. The asymmetry of pursuit associated with latent nystagmus is more marked at the onset than during maintenance.\(^{454}\) Furthermore, if moving stimuli are briefly presented after pursuit is underway, nasalward and temporalward image motion is equally effective in modulating eye velocity.\(^{239}\) This suggests that defect is more related to pursuit initiation than maintenance. Vertical optokinetic stimulation induces nystagmus with an inappropriate horizontal component, which cannot be accounted for by ongoing latent nystagmus, and which probably reflects maldevelopment of motion processing mechanisms.\(^{161}\)

Insights into the pathogenesis of latent nystagmus have been provided by studies of monkeys reared under a range of experimental conditions that preclude normal development of binocular vision. Thus, surgically creating strabismus in the first two months of life causes latent nystagmus.\(^{239}\) Electrophysiological studies indicate that neurons in MT in such strabismic monkeys have normal responses but are rarely driven binocularly. Binocular lid suture for the first 25–40 days of life also causes strabismus, latent nystagmus, and asymmetric optokinetic responses that affect optokinetic after-nystagmus, which implies disturbance of the velocity-storage mechanism (which is discussed in Chapter 2).\(^{451,452}\) How can these results be explained?

The activity of neurons in the nucleus of the optic tract (NOT) of adult monkeys raised with binocular eyelid sutures during the first days of life shows a large proportion of units that are dominated by the contralateral eye, in contrast to normal animals in which NOT units are sensitive to stimuli to either eye.\(^{339}\) Furthermore, some NOT neurons respond preferentially to contraversive visual motion, which is rare in NOT of normal monkeys, where most neurons are sensitive to ipsiversive visual motion. Pharmacological inactivation of NOT with muscimol abolishes latent nystagmus in these monkeys. Thus, NOT appears to play an important role in the generation of latent nystagmus as well as asymmetric monocular optokinetic responses in monkeys raised with binocular lid sutures. However, more than one mechanism seems likely. Thus, if bilateral lid sutures are extended to 55 days, pendular nystagmus also occurs. Moreover, if infant monkeys are reared with an opaque contact lens over one eye that is alternated daily, they develop strabismus, but no latent nystagmus or optokinetic abnormalities. In such monkeys, neurons in primary visual cortex (V1), but not in visual area MT, lack binocular responses.\(^{352}\) Monkeys reared in a 3-Hz strobe environment, which prevents visual image motion, develop pendular nystagmus but no strabismus. Finally, for latent nystagmus to develop, some residual binocular vision is probably necessary (which is possible through thin eyelids if the tarsal plate is removed). Thus, it appears that disruption of sensory fusion during infancy causes strabismus and, if some form of vision from each eye is present, NOT responses become monocular, which causes optokinetic deficits and latent nystagmus. Pendular nystagmus develops in infant monkeys deprived of visual motion information.\(^{452}\)

Despite this body of evidence, it remains possible that other factors such as abnormal extraocular proprioception,\(^{212}\) or disturbance of either directed visual attention or egocentric localization play a role in the pathogenesis of LN.\(^{114,246}\) Thus, some subjects can change direction of their nystagmus by “attempting” to view with one or the other eye, without change in visual inputs. Further discussion may be found in the section on latent nystagmus in Chapter 10.

### Smooth Pursuit in Patients with Infantile Nystagmus Syndrome (Congenital Nystagmus)

Some individuals with congenital nystagmus (see Video Display: Congenital Forms of Nystagmus) maintain adequate “foveation periods” (periods when the image of the target is close to the fovea and eye velocity is similar to target velocity) during smooth pursuit.\(^{116}\) Other individuals pursue poorly, probably because of associated visual defects rather than the congenital nystagmus per se. Finally, some affected individuals respond to a step-ramp pursuit stimulus with a reversal of their nystagmus slow phase that is in the direction opposite to the target ramp (see Video Display: Disorders of Smooth Pursuit).\(^{232}\) Some individuals with congenital nystagmus seem to...
show an “inversion of smooth-pursuit or optokinetic responses.” For example, when they watch a hand-held optokinetic drum, the quick phases are directed to the same side as that to which the drum rotates. It has been shown, however, that the velocity of the moving optokinetic stimulus does not influence the slow-phase velocity of the nystagmus. One interpretation of this last phenomenon is that smooth pursuit causes the nystagmus null point (i.e., orbital eye position at which eye velocity is zero) to shift to some other point. An alternative explanation is that, in some individuals, velocity feedback signals due to proprioception or efference copy are processed incorrectly, with an inversion of sign, leading to a wrongly directed smooth pursuit command.

Recent surgical therapies for congenital nystagmus are based on the notion that disrupting proprioceptive feedback, by severing and then reattaching the extraocular tendons from the eye, will diminish the ocular oscillations.

“Inversion of optokinetic responses” has also been found in albino rabbits when stimulation was limited to the anterior visual field (temporal retina). Such animals showed a spontaneous nystagmus when their posterior visual fields were covered. A variety of albino species show anomalies of their visual pathways. Evidence for abnormal decussation of temporal retinal fibers has been found in patients with ocular albinism. Congenital nystagmus is a cardinal feature of human albinism. Absence of crossing of nasal fibers in achiasmatic patients, or mutant sheep dogs, is associated with congenital seesaw nystagmus. The relationship between this misrouting of the visual pathways and congenital nystagmus has yet to be determined. However, it has been suggested that the pendular form of congenital nystagmus (discussed further in Chapter 10) may arise from oscillations within the pursuit system itself.

SUMMARY

1. Smooth pursuit eye movements enable continuous clear vision of objects moving within the environment. Smooth pursuit may have evolved to provide continuous foveal vision of a stationary object during self-motion. There is some evidence for separate neural mechanisms that are more concerned with either visual fixation of a stationary target or smooth pursuit of a target that moves.

2. The principal stimulus for pursuit eye movements is the motion of the image of a target across the retina and especially the foveal and perifoveal region. Under certain circumstances, the perception of image motion may be sufficient, and even nonvisual stimuli such as proprioception can also generate smooth tracking movements. Smooth-pursuit responses are greatly influenced by the predictability of target motion.

3. Smooth pursuit can be quantified by measuring its onset and its maintenance. Step-ramp stimuli, presented in a non-predictable sequence, can be used to measure the onset of smooth pursuit and especially the open-loop response, which is a sensitive index of pursuit malfunction. Step-ramp stimuli also permit one to assay the contribution of a specified portion of the retina (visual field) to the generation of the pursuit response. During maintenance of smooth pursuit, gain (eye velocity/target velocity) is the most useful measurement. If sinusoidal stimuli are used, the effects upon gain of increasing peak velocity and peak acceleration of the stimulus can be determined.

4. Like other classes of eye movements, smooth pursuit is under adaptive control, even though it uses visual feedback. Pursuit adaptation becomes evident following ocular nerve palsy. Experimental studies have shown that cortical areas concerned with motion vision play a key role in the adaptive response.

5. The pursuit pathway (Fig. 6–8) begins with a visual subsystem for analyzing movement; it starts at the retina and runs to the magnocellular portion of the lateral geniculate nucleus, the striate cortex, secondary visual areas (MT and MST), the dorsolateral pontine nucleus, cerebellum, vestibular nuclei, brainstem reticular formation, and the ocular motor nuclei. Study of discrete lesions along this pathway has provided insight into visual processing of moving targets. Unilateral lesions along this pathway pro-
duce a predominantly ipsilateral deficit of smooth pursuit. The frontal and supplementary eye fields also contribute to smooth pursuit, and may be important in generating responses to predictable target motions. An accessory optic system and the nucleus of the optic tract may play a role in activating the transcortical-pontine-cerebellar pursuit pathway Figure 4–8.

6. The pursuit response shows considerable inter-subject variability. Pursuit is influenced by alertness and by a variety of drugs, and declines in old age. Impaired pursuit (reduced gain) is a nonspecific finding of many diffuse neurologic disorders. Cortical lesions cause distinct deficits of smooth pursuit (Fig. 4–12). Abnormalities of smooth pursuit may be encountered in some individuals with congenital forms of nystagmus, and provide insights into the underlying mechanisms.

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