Chapter 1

A Survey of Eye Movements: Characteristics and Teleology

WHY STUDY EYE MOVEMENTS?

The study of eye movements is a source of valuable information to both basic scientists and clinicians. To the neurobiologist, the study of the control of eye movements provides a unique opportunity to understand the workings of the brain. To neurologists and ophthalmologists, abnormalities of ocular motility are frequently the clue to the localization of a disease process. Moreover, the visual and perceptual consequences of eye movements are important to both basic scientists and clini-

cians. Over the past three decades, eye movements have increasingly been applied as an experimental tool to gain insight into disorders ranging from muscular dystrophy to dementia.[40,46] Eye movements have even been used to address fundamental issues of human behavior, such as free will and conflict resolution, as subjects respond to visual targets while their frontal lobe activity is monitored by functional magnetic resonance imaging (fMRI) (see Fig. 1–7).[59] And careful clinical observations combined with genetic linkage studies have provided insights into the nature of dis-

eases as diverse as myopathy and cerebellar ataxia.[49,82] Eye movements are also being used to identify and test new therapies for a range of genetic and degenerative disorders.[72] In fact, recent functional imaging studies in human beings and recordings of activity of single neurons in monkeys performing in sophisticated behavioral paradigms have shown that activity related to eye movements can be found in almost every corner of the brain. This should come as no surprise, because we are creatures who depend upon clear vision, and must focus our attention to make prompt, correct responses to what is happening around us. Eye movements both reflect and facilitate this central role for vision in survival.

The singular value of studying eye movements stems from certain advantages that make them easier to interpret than movements of the axial or limb musculature. The first advantage is that eye movements are essentially restricted to rotations of the globes; translations (linear displacements) are negligible. This facilitates precise measurement (Fig. 1–1 and Appendix B), which is a prerequisite for quantitative analysis. A second advantage is the apparent lack of a classic, monosynaptic stretch reflex.[41] This is not unexpected because the eye muscles move the globe against an unchanging mechanical load. Third, different classes of eye movements (Table 1–1) can be distinguished on the basis of how they aid vision, their physiological properties, and their anatomical substrates. Fourth, many abnormalities of eye movements are distinctive and often point to a specific pathophysiology, anatomical localization, or pharmacological disturbance. Finally, eye movements are readily accessible to observation and systematic examination. For this reason, we provide a DVD with Video Displays, and individual video clips, which we hope will immediately bring to life the nature of a disorder being discussed in the text. This chapter provides an overview of the normal behavior of eye movements, and introduces the reader to some current concepts of the underlying neural control. We start by examining why the eyes must move at all—the *raison d'être* of eye movements.[25,69,86a,89]

Figure 1–1. The scleral search coil method for precise measurement of horizontal, vertical, and torsional eye rotations. The subject is wearing a silastic annulus in which are embedded two coils of wire, one wound in the frontal plane (to sense horizontal and vertical movements) and the other wound in effectively the sagittal plane (to sense torsional eye movements). When the subject sits in a magnetic field, voltages are induced in these search coils that can be used to measure eye position (see Appendix B for details).

Table 1–1. **Functional Classes of Human Eye Movements**

Class of Eye Movement	Main Function
Vestibular	Holds images of the seen world steady on the retina during brief head rotations or translations
Visual Fixation	Holds the image of a stationary object on the fovea by minimizing ocular drifts
Optokinetic	Holds images of the seen world steady on the retina during sustained head rotation
Smooth Pursuit	Holds the image of a small moving target on the fovea; or holds the image of a small near target on the retina during linear self-motion; with optokinetic responses, aids gaze stabilization during sustained head rotation
Nystagmus quick phases	Reset the eyes during prolonged rotation and direct gaze towards the oncoming visual scene
Saccades	Bring images of objects of interest onto the fovea
Vergence	Moves the eyes in opposite directions so that images of a single object are placed or held simultaneously on the fovea of each eye

VISUAL REQUIREMENTS OF EYE MOVEMENTS

What visual needs must eye movements satisfy? To answer this question, we must first identify the prerequisites for a clear and stable view of the environment. Simply stated, clear vision of an object requires that its image be held fairly steadily on the central, foveal region of the retina. Otherwise visual acuity declines and patients may experience oscillopsia— illusory movement of their visual environment (see Video Display: Treatments for Nystagmus).

Just how steadily must images of the world be held on the retina for vision to remain clear and stable? The amount of retinal image motion that can be tolerated before vision deteriorates depends upon what is being viewed, and specifically, its spatial frequency. For objects with higher spatial frequencies, such as the Snellen optotypes used for conventional testing, retinal image motion should be held below about 5 degrees per second; above this threshold, visual acuity declines in a logarithmic fashion.[7,15] An exception to these general rules concerns eye rotations about the line of sight—torsional movements when the subject views a small object with the fovea; in this case, geometry dictates that horizontal and vertical components of retinal image motion will remain relatively small.

For clearest vision of a single feature of the world, its image must not only be held fairly steady on the retina, but must also be brought close to the center of the fovea, where photoreceptor density is greatest. Visual acuity declines steeply from the fovea to the retinal periphery.[15,39] For example, at 2 degrees from the center of the fovea, visual acuity has declined by about 50%. For best vision, the image of the object of regard should be within 0.5 degrees of the center of the fovea. Thus, during visual search of the environment, the fovea must be pointed at features of interest (Fig. 3–8A, Chapter 3).[91]

Under normal circumstance, the angle of gaze (which corresponds to eye position in space and the line of sight) is held steadily enough that our perception of the world is clear and stationary. The normal, small movements of the eyes that occur as we fix upon an object (Figs. 1–2A) do not interfere with clear vision, and may actually enhance it.[53,81] However, when disease causes abnormal oscillations of the eyes, such as nystagmus (Fig. 1–2B), the images of stationary objects move excessively on the retina and patients report blurring of vision and oscillopsia (see Video Display: Treatments for Nystagmus).

FUNCTIONAL CLASSES OF EYE MOVEMENTS

Since our eyes (and retinas) are attached to our heads, the greatest threat to clear vision during
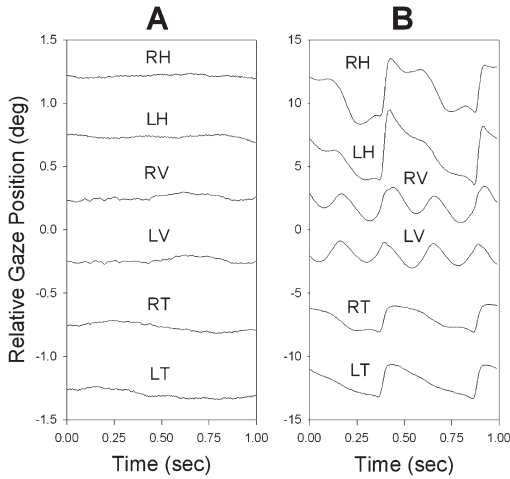
Figure 1–2. Normal and abnormal eye movements during attempted visual fixation of a stationary target. (A) One-second, representative record of the gaze of a normal subject. (B) One-second record from a 35-year-old woman with multiple sclerosis, in whom acquired pendular-jerk nystagmus (see Video Display: Treatments for Nystagmus) precluded steady fixation. Her main complaints were that she could not see clearly and that the world appeared to be moving (oscillopsia) in a direction corresponding to that of her nystagmus. Measurements were made using the magnetic search coil technique. RH: right horizontal; LH: left horizontal; RV: right vertical; LV: left vertical; RT: right torsional; LT: left torsional. Note that gaze positions are relative, having been offset to aid the clarity of the display, and that the scales differ by a factor of 10. Polarity: positive = right, up, or clockwise.

natural behavior is head perturbations, especially those that occur during locomotion (Fig. 7–1).[33,56] If we had no eye movements, images of the visual world would "slip" on the retina with every such head movement. This would cause our vision to become blurred and our ability to recognize and localize objects to be impaired whenever we moved through the environment. To this end, two distinct mechanisms evolved to stabilize images on the retina in general, and the fovea in particular, during such head perturbations. The first comprises the vestibulo-ocular reflexes, which depend on the ability of the labyrinthine mechanoreceptors to sense head accelerations. The second consists of visually-mediated reflexes (optokinetic and smooth-pursuit tracking), which depend on the ability of the brain to determine the speed of image drift on the retina. Together, these reflexes *stabilize the angle of gaze*, so that the fovea of each eye remains pointed at the object of regard whenever the head is moving.

With the evolution of the fovea, a second requirement of eye movements also arose: when a new object of interest appears in the visual periphery, we need to point this central portion of the retina so that the object can be seen best. This requires a repertoire of eye movements to *change the angle of gaze*. In animals without a fovea, such as the rabbit, eye movements are dominated by vestibular and optokinetic stabilization. When such animals choose to change their center of visual attention, they must link a rapid eye movement to a voluntary head movement and so override or cancel vestibular and optokinetic drives. With the emergence of foveal vision, it became necessary to change the line of sight independently of head movements. In this way, images of objects of interest could be brought to and held on that portion of the retina providing best visual acuity. With the evolution of frontal vision and binocularity, disjunctive or vergence eye movements also became necessary, so that images of an object of interest could be placed on the fovea of each eye simultaneously, and then held there.

Thus, eye movements are of two main types: those that stabilize gaze and so keep images steady on the retina, and those that shift gaze and so redirect the line of sight to a new object of interest.[9,16] The chief functional classes of eye movement are summarized in Table 1–1. Each functional class has properties suited to a specific purpose.[25,69,89] Moreover, as detailed in the following chapters, certain anatomical circuits make distinctive contributions to each functional class of movements. An understanding of the properties of each functional class of eye movements will guide the physical examination; knowledge of the neural substrate will aid topological diagnosis. But before discussing each of these various classes of eye movement, we must first examine the mechanical properties imposed on the eye by its surrounding tissues and muscles. The brain must deal with these mechanical factors in order to program fluent and accurate eye movements.

ORBITAL MECHANICS: PHASIC AND TONIC INNERVATION

The tissues supporting the eyeball impose mechanical constraints on the control of gaze. To move the eye, it is necessary to overcome
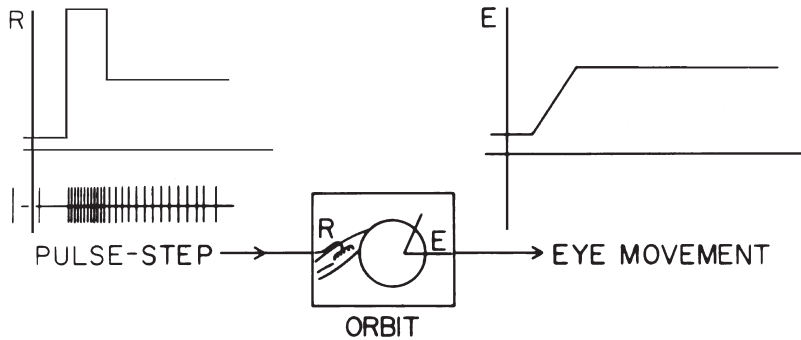
Figure 1–3. The neural signal for a saccade. At right is shown the eye movement: E is eye position in the orbit; the abscissa scale represents time. At left is shown the neural signal sent to the extraocular muscles to produce the saccade. The vertical lines indicate the occurrence of action potentials of an ocular motoneuron. The graph above is a plot of the neuron's discharge rate (R) against time (firing frequency histogram). It shows the neurally encoded pulse (velocity command) and step (position command).

viscous drag and elastic restoring forces imposed by the orbital supporting tissues. To overcome the viscous drag, a powerful contraction of the extraocular muscles is necessary. For rapid movements (e.g., a saccade), this requires a phasic increase or burst of neural activity in the ocular motor nuclei*—the pulse of innervation (Fig. 1–3). Once at its new position, the eye must be held there against elastic restoring forces that tend to return the globe to its central position. To hold the eye in an eccentric position requires a steady contraction of the extraocular muscles, arising from a new tonic level of neural activity—the step of innervation. (For a demonstration of the elastic forces acting on the eyeball, see Video Display: Disorders of Gaze Holding.) When this pulse-step of innervation is appropriately programmed, the eye is moved rapidly to its new position, and held there steadily. (For an audiovisual example of ocular motoneuron activity during saccades, see Video Display: Disorders of Saccades.) Some of the first studies of the discharge characteristics of ocular motoneurons (see Fig. 5–2, Chapter 5) in monkeys,[27,67,70,74] and of eye muscles in human beings (see Fig. 9–6, Chapter 9),[19] confirmed the presence of both the pulse and step of innervation during saccades.† Without the pulse (velocity command), the progress of the eye would be slow; without the step (position command), the eyes could never be maintained in an eccentric position in the orbit. Moreover, the pulse and step must be correctly matched to produce an accurate eye movement and steady fixation following it. These concepts are important for interpreting clinical disorders of eye movements, such as internuclear ophthalmoplegia, when there is a pulse-step mismatch that causes the adducting eye to drift slowly to the target (see Video Display: Pontine Syndromes).

Although our discussion so far has concerned the generation of saccades, the same considerations about mechanical properties of the orbit apply to the commands for all types of eye movement. Studies of the activity of ocular motor neurons in alert monkeys have shown that the neural commands for all conjugate movements (vestibular, optokinetic, saccadic, and pursuit) and for vergence movements have both velocity and position components.[57,85,87] How are the velocity and position components of the ocular motor commands synthesized?

Neurophysiological evidence indicates that the position command (e.g., for saccades, the step) is generated from the velocity command (e.g., for saccades, the pulse) by the mathematical process of integration with respect to time. A neural network integrates, in this mathematical sense, velocity-coded signals into position-coded signals; this network is

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*We use the term "ocular motor" to refer to the eye movement control system as a whole, or the third, fourth, and the sixth cranial nerves or their nuclei collectively, and "oculomotor" to indicate the third nerve or its nucleus alone.

†In fact, the mechanical properties of the orbital contents dictate the need for a more complicated ocular motor command, namely a pulse-slide-step, which is discussed in Chapter 5.

referred to as the neural integrator.[2,77] When this process is faulty, the eye is carried to its new position by the pulse but cannot be held there and drifts back to the central position. This is evident clinically as gaze-evoked nystagmus (see Video Display: Disorders of Gaze Holding). Since all types of conjugate eye movements require both velocity-coded and position-coded changes in innervation, all conjugate eye movement commands need access to a common neural integrator. Experimental lesions of structures vital for neural integration affect all classes of conjugate eye movements.[2,13] Furthermore, it appears that vergence eye movements are also synthesized from velocity and position commands, the latter generated by a vergence integrator.[29]

The past decade has witnessed a revolution in our concepts of the organization of the extraocular muscles and the orbital tissues.[23] Current evidence indicates that each extraocular muscle consists of outer orbital and inner global layers, each with special fiber types that endow properties such as fatigue resistance. The outer orbital layer inserts not into the eyeball but into a fibrous pulley, which acts as the functional point of origin for the global layer that passes through and inserts onto the globe (Fig. 9–1). In Chapter 9 we discuss the functional implications of the orbital pulleys, and the contribution they make to determining the axes about which the eyes rotate.[22,32]

$$EYE_{space} = EYE_{orbit} + HEAD_{space}$$

Figure 1–4. The angular vestibulo-ocular reflex (VOR). As the head is rapidly turned to the left, the eyes move by a corresponding amount in the orbit to the right. Below, head position in space and eye position in the orbit are plotted against time. Because the movements of head and eye in orbit are equal and opposite, the sum, eye position in space (the angle of gaze or "gaze"), remains zero (bottom equation). If gaze is held steady, images do not slip on the retina and vision remains clear. During viewing of targets at optical infinity, eye rotations are equal and opposite to head rotations. During viewing of near targets, eye rotations are greater than head rotation, because the eyes do not lie in the center of the head (see Chapters 2 and 7).

VESTIBULAR AND OPTOKINETIC SYSTEMS

The Vestibulo-Ocular Reflex: Responses to Brief Angular and Linear Head Movements

The vestibular system stabilizes gaze and ensures clear vision during head movements, especially those that occur during locomotion. Vestibular eye movements are generated much more promptly (i.e., at shorter latency) than are visually mediated eye movements. This is because the acceleration sensors of the labyrinth signal motion of the head much sooner than the visual system can detect motion of images on the retina. Thus, the vestibulo-ocular reflex (VOR) (Fig. 1–4) ge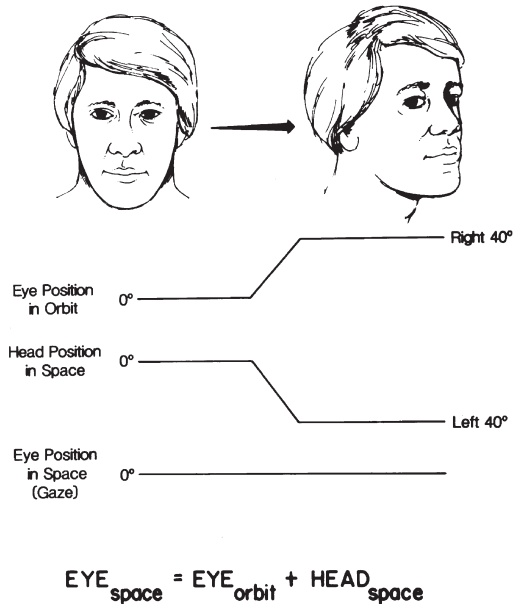nerates eye movements to compensate for head movements at a latency of less than 15 ms,[52,64,83] whereas visually mediated eye movements are initiated with latencies greater than 70 ms.[31] This difference becomes an important issue during locomotion because the head perturbations that occur with each footfall contain predominant frequencies ranging from 0.5 to 5.0 Hz.[20,33] Only the short-latency VOR is fast enough to generate eye movements to compensate for head perturbations at these frequencies. This becomes clinically evident in patients who have lost labyrinthine function, who complain, for example, that they cannot read street signs while they are in motion.[38] (For a demonstration of the visual consequences of losing the VOR see Video Display: Disorders of the Vestibular System.)

Although the VOR acts independently of visually mediated eye movements, the brain continuously monitors its performance by eval-

uating the clarity of vision during head movements. Thus, an appropriately sized eye movement must be generated by the VOR in order for the angle of gaze (eye position in space) to be held steady and the image of the world to remain fairly stationary upon the retina (Fig. 1–4). If it is not, then the performance of the VOR undergoes adaptive changes to restore optimal visuo-motor performance.

The vestibular system can respond to movements that have angular (rotational) or linear (translational) components.[1,20] The angular VOR (Fig. 1–4) depends on the semicircular canals, of which there are three in each inner ear (see Fig. 2–1). In health, the semicircular canals work together to sense head rotations in any plane. Thus, the angular VOR stabilizes images on the retina during head rotation. However, when disease affects an individual semicircular canal, spontaneous eye movements (nystagmus) occur in the plane of that canal, reflecting a common evolutionary relationship between individual semicircular canals and the pulling directions of the extraocular muscles.[18,76] An appreciation of this fundamental physiologic and anatomic feature of vestibulo-ocular control helps one interpret various patterns of nystagmus observed in vestibular disease. For example, in the common disorder, benign paroxysmal positional vertigo that affects the posterior semicircular canal, nystagmus consists of eye rotations in the plane of the affected canal (see Video Display: Disorders of the Vestibular System). Because the eyes are not at the center of rotation of the head, but are situated eccentrically, in the orbits, pure head rotations also produce translations, or linear displacements, of the eye. This geometry becomes important if head rotations occur during viewing of a near object, when the brain must independently adjust the size of movements of each eye so that they can remain pointed at the object of regard.

The translational VOR (Fig. 1–5) depends on otolithic organs, the utricle and the saccule (see Fig. 2–1, bottom).[1] Otolithic-ocular reflexes become important if a subject views a near object, when they generate eye rotations to compensate for translation of the head, including the orbits, which house the eyes.[56] The translational VOR is essentially a binocular foveally driven reflex. Its function is to stabilize images upon the fovea of both eyes and so must tailor its response to the point of inter-
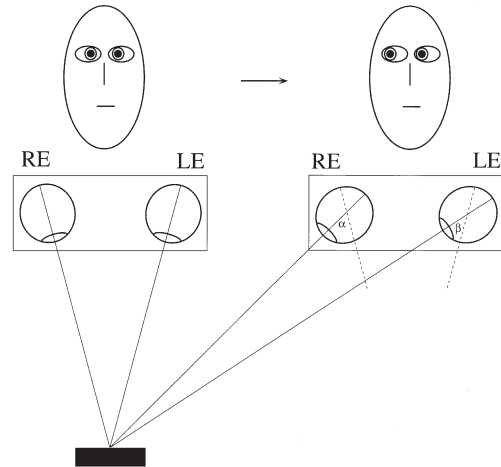

Figure 1–5. The translational VOR. Before the head movement (left panel), both the right eye (RE) and left eye (LE) fix on a stationary, near target, which requires convergence. As the subject's head translates to his left (arrow), a compensatory eye rotation movement to the right is generated. After the head movement (right panel), note that the right eye has rotated through a larger angle (α) than the left eye (β) because of the asymmetry of the geometric relationship between each eye and the target. Eye rotations are only necessary to compensate for head translations while viewing near targets.

section of the lines of sight of each eye in three-dimensional space. Natural head movements have both rotational and translational components; the eye rotations to compensate for them may have horizontal and vertical components, and must be appropriate for the viewing distance of the visual scene.

Eye Movements in Response to Sustained Rotations: The Optokinetic System

Although the labyrinthine semicircular canals reliably signal transient head rotations, their Achilles' heel is a sustained (low frequency) rotation, which they signal progressively less accurately because of the mechanical properties of the semicircular canals. If a subject is rotated in darkness at a constant velocity, the slow phases of vestibular nystagmus, which are initially compensatory, decline in velocity and, after about 45 seconds, the eyes become stationary (Fig. 1–6). Sustained rotation may occur naturally as a component of a sustained chase, and the declining vestibular responses
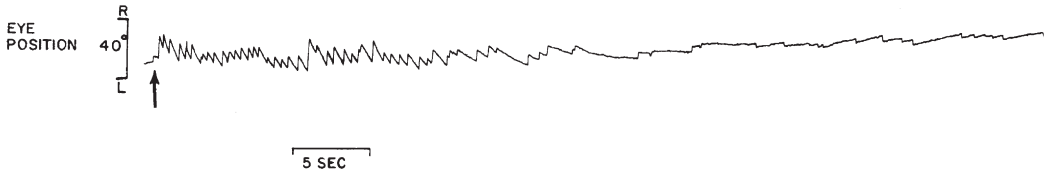
Figure 1–6. Record (D.C. electrooculography) of the vestibulo-ocular response to sustained rotation. Horizontal eye position is plotted against time. At the arrow, the subject starts to rotate clockwise, in darkness, at 50 degrees per second, and this velocity is maintained throughout the record. Initially there is a brisk nystagmus consisting of vestibular slow phases that hold gaze steady during the head rotation, and quick phases that not only reset the eyes to prevent them from lodging at the corners of the orbit but move them into the direction of head rotation. After about 30 seconds of rotation, the nystagmus (i.e., the vestibular response) dies away. Because of the mechanical limitations of the semicircular canals, the motion detectors cannot accurately inform the brain about sustained rotations. Eventually, nystagmus develops in the opposite direction (reversal phase); this represents the effect of short-term vestibular adaptation, a phenomenon discussed in Chapter 2. Upward deflections indicate rightward eye movements.

would, if acting alone, lead to degradation of vision and so threaten survival. Hence there is a need for alternative means of stabilizing retinal images to supplant the fading vestibular response. Visually mediated eye movements can serve this function, because sustained responses do not require a short latency of action. In afoveate animals, such as the rabbit, visually mediated eye movements can only be driven if the entire visual scene moves—the optokinetic response. However, in foveate, frontally eyed animals, both behavioral and neurophysiological evidence suggests that smooth-pursuit eye movements are mainly responsible for holding gaze on an object during self-motion.[56] The supplementation of the VOR by visually mediated eye movements is more than a summation of responses that are generated independently. For example, in the vestibular nuclei of the monkey, some neurons are driven by both visual (optokinetic) and vestibular stimuli (Fig. 2–5, Chapter 2), implying a "neural symbiosis."[68,87] As the labyrinthine signal declines, visual drives take over and maintain compensatory slow-phase eye movements during sustained rotation.

Visually mediated eye movements also supplement the translational VOR, when the visual scene is close to the subject.[8,88] In this case, smooth-pursuit eye movements are important, because they allow steady fixation of a small, near target, the position of which changes with respect to the background, as the subject translates. If we view distant objects, no eye movements are needed to compensate for head translations but, no matter what the viewing distance, eye movements are always needed to compensate for head rotations.

SACCADIC SYSTEM

Quick Phases

Most head movements are brief and require only small compensatory eye movements to maintain the stability of gaze. Any sustained head rotation would, however, cause the eyes to lodge at the corners of the orbit, in extreme contraversive deviation, where they no longer could make appropriate movements. This is not normally observed because of corrective quick phases (Fig. 1–6). These rapid eye movements, the evolutionary forerunners of voluntary saccades, have been likened to a resetting mechanism for the eye. In fact they do more than this because, during head rotation, quick phases move the eyes in the orbit in the same (anti-compensatory) direction as that of head rotation (Fig. 1–6) and so enable perusal of the oncoming visual scene.[55] Quick phases of nystagmus are rapid, with maximal velocities as high as 500 degrees per second, repositioning the eye in the shortest time possible.[30] The anatomic substrate of these rapid eye movements is in the paramedian reticular formation of the pons and mesencephalon (Fig. 6–3, Chapter 6), the same as that for saccades.[10] In disorders in which the quick-phase mechanism fails, the eyes hang up at the extremes of the orbit (see Video Display: Congenital Ocular Motor Apraxia).

Voluntary Saccades

Foveate animals have developed the ability to redirect the line of sight even in the absence of

head movements: they have both quick phases and voluntary saccades. With the evolution of the fovea, it became important to be able to direct this specialized area of the retina at the object of interest during visual search. Saccades may be triggered in day-to-day life by objects actually seen or heard, or from memory, or as part of a natural strategy to scan the visual scene. There is usually a delay of about 200 ms from the stimulus for a saccade until its enactment, and this time presumably includes neural processing in the retina, cerebral cortex, superior colliculus, and cerebellum (see Voluntary Eye Movements, below). The final neural instruction for voluntary saccades arises from the same brainstem neurons in the paramedian reticular formation that generate the quick phases of nystagmus. Normal saccades are fast, brief, and accurate, so they do not interfere with vision. Disease may cause them to become slow, prolonged, or inaccurate, when they may cause visual disability (for example, see Video Display: Disorders of Saccades).

SMOOTH PURSUIT AND VISUAL FIXATION

Smooth Pursuit

With the evolution of a fovea has also come the need to track a moving object smoothly. This is possible to only a limited degree with saccadic movements, since once captured on the fovea by a saccade, the image of the moving target soon slides off again, with a consequent decline in visual acuity. The pursuit system, however, generates smooth tracking movements of the eyes that closely match the pace of the target. To overcome the delays inherent in the visual system (the latency of responses, which ranges between 80 ms − 120 ms), predictive mechanisms can adjust the eye movements when the motion of the target can be anticipated.[4] It seems possible that smooth-pursuit eye movements evolved in response to the need to sustain foveal fixation on a near target during self-motion (translation).[56] In this case, to compensate for movement of the head, the visual system would need to generate eye movements appropriate for the proximity of the near target, and relative motion between the near target and background.

Factors other than vision can be used to generate pursuit, because some normal subjects can follow their own fingers in darkness.[80] In fact, the brain relies on a number of sensory inputs, and its own motor efforts, to determine the motion of the target of interest. Smooth pursuit performance declines with age, and as a side effect of many drugs with effects on the nervous system, and thus, alone, impaired pursuit does not allow accurate localization of a disease process. Recent studies of visual processing in cerebral cortex, and the effects of discrete lesions, have clarified much about the neural substrate of smooth pursuit, and have suggested than some of the organization of the pursuit system has similarities with other voluntary eye movements, such as saccades.[43] Diseases that disrupt smooth pursuit do not usually cause visual disability, but they can provide valuable diagnostic information (see Video Display: Disorders of Smooth Pursuit).

Visual Fixation

Visual fixation of a stationary target may represent a special case of smooth pursuit—suppression of image motion caused by unwanted drifts of the eyes,[91] but it might also be due to an independent visual fixation system.[50] Such a mechanism would reflect the ability of the visual system to detect retinal image motion caused by unwanted drifts of the eyes and program corrective movements. Especially in the wake of a saccade, moving, large-field textured stimuli can induce ocular following at a latency of about 70 ms.[31] These ultra-short latency responses are driven by first-order visual stimuli, defined by the spatial distribution of luminance, and are not dependent on the attentive state of the subject.[17] Thus, short-latency ocular following is probably an important component of the fixation mechanism.

Another aspect of steady fixation is the ability to suppress saccadic eye movements that turn the fovea away from the object of interest. Thus, certain neurons in the frontal eye fields and superior colliculus seem important for suppressing saccades when steady fixation of a target (e.g., threading a needle) is necessary.[5,37,81] The concept of a fixation system becomes important in certain disease states. For example, following a peripheral vestibular lesion, the nystagmus is "suppressed" if visual

fixation of a stationary object is possible. On the other hand, unwanted saccades may intrude on steady fixation, for example, as opsoclonus (see Video Display: Saccadic Oscillations and Intrusions).

Similarities and Differences between Fixation, Smooth-Pursuit, and Optokinetic Eye Movements

We have described three situations in which smooth, sustained eye movements may be made in response to motion of images across the retina. When such eye movements are in response to viewing the whole visual scene during sustained self-rotation, we have referred to them as optokinetic. When they oppose drifts of the eyes directed away from a stationary target, we have called them fixation. And when they are used to smoothly follow a moving object, or maintain fixation on a near, stationary target during self-motion, we have used the term smooth pursuit. In each of these cases, areas of cerebral cortex extract information about the direction and speed of retinal image slip from each eye, so that brainstem and cerebellar circuits can program an eye movement. The overlap and interaction between these types of eye movements are discussed in later chapters. Here, however, we have presented them as three different functional classes of eye movements because of their different purposes and properties, which lead to distinct methods of testing during clinical and laboratory examinations.

COMBINED MOVEMENTS OF THE EYES AND HEAD

The study of eye movements with the head held stationary is useful for investigative purposes but is artificial because, during natural behavior, humans usually move their eyes and head together. We have already indicated how vestibular responses compensate for the head perturbations due to locomotion. Such vestibular drives, however, may become an encumbrance when voluntary changes of the angle of gaze (eye position in space), using the eyes and head, are required. For example, if we are *smoothly* tracking a target moving to the right

with a combined movement of the eyes and head, the eyes would continually be taken off target to the left if the VOR went unchecked. In fact, however, the eyes remain relatively stationary in the orbit as if the VOR were turned off. This implies an ability to override those vestibular drives invoked by voluntary head movements made to track a moving target. Current evidence suggests that two mechanisms contribute: (1) the VOR signal is canceled by an oppositely directed smooth-pursuit signal; (2) there is a parametric adjustment of the magnitude (gain) of the VOR response itself.[21] Thus, disorders that disrupt smooth pursuit often also interfere with smooth eye-head tracking (see Video Display: Disorders of Smooth Pursuit).

During *rapid* gaze changes, achieved with the eyes and head, saccadic and vestibular signals are appropriately combined so that gaze is accurately redirected toward the desired target; this may be achieved by either adding the two oppositely directed signals or by effectively "disconnecting" the VOR.[45] Which process takes place may depend partly upon the size of the gaze change.[84] Especially for larger movements that exceed the ocular motor range, disconnecting the VOR may be the major strategy.[54,83] Patients who have difficulty generating saccades with their eyes alone often make a combined eye-head movement to generate a gaze-shift (see Video Display: Acquired Ocular Motor Apraxia).

VERGENCE EYE MOVEMENTS

With the development of frontal vision it became possible to direct the fovea of both eyes at one object of interest. This requires disjunctive or vergence movements that, in contrast to conjugate or visional movements, move the eyes in opposite directions. Two principal types of stimulus drive vergence eye movements: image disparity and image blur. *Disparity or fusional vergence* movements occur in response to disparity between the locations of images of a single target on the retina of each eye. This type of vergence eye movement may be elicited at the bedside by placing a wedge prism before one eye. *Accommodative vergence* is stimulated by loss of focus of images (blur) on the retina and occurs in association with accommodation of the lens and pupillary

constriction, as part of the near triad. Accommodative effort alone can produce vergence movements. Thus, if one eye is covered and the other eye suddenly changes fixation from a distant to a near target, then the eye under cover responds by converging. A similar effect may be induced by placing a negative diopter (minus) lens in front of the viewing eye. Other stimuli are also important inputs for vergence, including the sense of nearness of the object of interest and a sense of motion of the target away from or towards oneself ("looming").

When vergence eye movements are performed alone, they are characteristically slow. During natural visual search, however, vergence movements are invariably accompanied by saccades, because the position of most objects in our environment differs in both direction (horizontal and vertical) and in distance (depth). When vergence movements are accompanied by near-synchronous saccades, they are speeded up, whereas the saccadic component is slowed down.[92] Since vertical saccades can speed up horizontal vergence, it seems most likely that these interactions between saccades and vergence occur centrally. Abnormalities of the vergence are responsible for many symptomatic ocular motor disorders, ranging from childhood strabismus to psychological spasm of convergence, to specific defects of vergence eye movements following brainstem strokes (see Video Display: Disorders of Vergence).[65]

THREE-DIMENSIONAL ASPECTS OF EYE MOVEMENTS

The eyes can rotate about any combination of three axes, which conventionally are described as X (parasagittal), Y (transverse), and Z (vertical) and intersect at the center of the globe (Fig. 9–3, Chapter 3). The orientation of the eye (i.e., the amount of torsion), at a given eye position, however, is governed by Listing's law, which confines the axes of eye rotation that describe eye position to a single plane— Listing's plane, which approximates the frontal plane (Fig. 9–3). The term "primary position" is now defined with reference to Listing's law. It is the unique position at which the line of sight is perpendicular to Listing's plane and the position from which purely horizontal or purely vertical rotations of the eye to a new position

are unassociated with any torsion. Primary position is usually close to but not necessarily exactly straight ahead. In this book, we use the term "central position" simply to denote that the eye is pointing straight ahead (visual axis is parallel to the midsagittal plane of the head). Measurements, using reliable methodology to measure 3-D rotations,[26] have confirmed that Listing's law is approximately obeyed for saccades and pursuit, but less so for vestibular movements in response to head rotations.[58] On the other hand, the eye movement responses to head translations do obey Listing's law, which probably reflects their close relationship to other foveally driven reflexes such as saccades and smooth pursuit.[88] These properties of eye rotations have been used to identify the pathogenesis of abnormal eye movements. For example, a form of nystagmus that obeys Listing's law would be more likely to arise from an abnormality within the pursuit system or translational VOR than from within the rotational VOR. In Chapter 9, we discuss further aspects of 3-D eye rotations, Listing's law and Donder's law, and the possible role of the extraocular muscle pulleys in enforcing it.

ADAPTIVE CONTROL OF EYE MOVEMENTS

To achieve clear, stable, single vision, the control of eye movements must be accurate. One of the most impressive aspects of ocular motor control is the way in which the brain constantly monitors its performance and, in the face of disease and aging, adjusts its strategies accordingly. For example, the performance of the VOR can be appropriately modified to new visual circumstances (e.g., a change in spectacle lens correction).[12,62] Furthermore, inaccurate saccades and deficient smooth pursuit caused, for example, by abducens nerve palsy can be corrected (see Video Display: Disorders of Smooth Pursuit).[60] Even the yoking of conjugate eye movements is under some degree of adaptive control.[3] The cerebellum plays a central role in recalibrating ocular motor reflexes for optimal visual performance,[66] using cues from cerebral cortical areas that process visual motion.[14] Within the cerebellum are a variety of neurons that influence eye movements. The vestibulocerebellum (flocculus, paraflocculus, and nodulus) is particularly important in the

control of smooth pursuit, in vestibular eye movements, and in holding positions of gaze.[6] The dorsal vermis (lobules V–VII) and underlying fastigial nucleus enable both saccades and pursuit to be accurate.[71] Thus, disease affecting the cerebellum may not only disrupt the control of eye movements, but also impair the individual's ability to correct them.

The adaptive repertoire consists of many levels of response to disease, from relatively low-level adjustments in innervation, to higher-level strategies that may depend upon the context in which they are elicited, such as reward in animal experiments.[24,42] So patients may develop different adaptive states that, based upon the context in which they must be elicited, allow for different innervational commands for the same type of eye movement.[75]

VOLUNTARY CONTROL OF EYE MOVEMENTS

The control of eye movements ranges from the most reflexive responses (e.g., a quick-phase of vestibular nystagmus) to eye movements that are willed without a sensory stimulus (e.g., a saccade made to a remembered or imagined location). Voluntary control of gaze depends upon a number of areas in cerebral cortex; their separate contributions have been elucidated by electrophysiological and lesion studies in monkeys. Homologous areas have been suggested in humans, based upon studies of either the behavioral effects of discrete lesions or functional imaging (see Fig. 6–8).

As a generalization, the anterior areas of cerebral cortex contribute more to the generation of voluntary, internally generated behaviors whereas posterior cortical areas play a more important role in more externally triggered reflexive behaviors. There is evidence that each cortical eye field may coordinate the components of more complex responses, for example, combined vergence-pursuit movements to targets moving smoothly in depth and direction.[28] From these cortical areas, parallel projections descend via the basal ganglion and superior colliculus to the brainstem and cerebellar circuits that fashion premotor eye movement commands.[36] Certain neurons in these pathways may encode mismatches between eye and target positions, which can be used to program more than one type of eye movement.[44] There is some redundancy of these pathways, so that lesions affecting one cortical area tend not to produce a permanent defect of voluntary gaze. Thus, independent lesions of either the frontal or parietal eye fields in monkeys produce subtle, chronic defects of saccadic eye movement control. However, combined lesions of these structures cause more severe and enduring limitation of ocular motility (see Video Display: Acquired Ocular Motor Apraxia).[51]

An important issue in the control of voluntary eye movements is the way that the brain transforms sensory signals into motor commands. Thus, visual stimuli are encoded in a place code, such as the topographic map of the visual fields in primary visual cortex. On the other hand, the ocular motoneurons encode the properties of an eye movement in their temporal discharge characteristics (Fig. 1–3). Thus, a spatial-temporal transformation of neural signals is required if, for example, a saccade is to be made in response to a visual target. The site and mechanism by which this transformation is achieved are subjects of present research, but cortical areas, the superior colliculus, cerebellum, and brainstem reticular formation may all contribute.

A recent trend has been to use eye movements to probe the highest cognitive functions such as conflict resolution and free will. By applying ingenious stimulus paradigms that provide visual stimuli with instructions that vary from trial to trial (such as a countermand after the stimulus is presented),[73] or by changing subsequent stimuli based upon eye movement responses, it has been possible to identify functional activation in parts of human pre-supplementary motor area (pre-SMA) and supplementary eye fields corresponding to volition, conflict, and registration of success or failure (Fig. 1–7).[59]

EYE MOVEMENTS AND SPATIAL LOCALIZATION

Since the eyes, head, and body can all move with respect to each other, the retinal location of an image cannot specify the position of the object in space. For this, information is required concerning the direction of gaze (eye
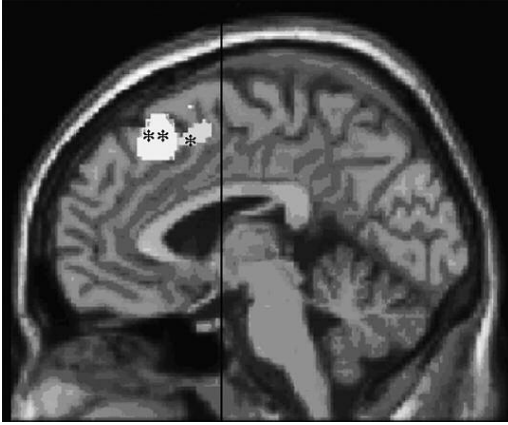
Figure 1–7. Pre-supplementary motor area (pre-SMA) activation associated with changing volitional plans (two asterisks or yellow) and free choice (one asterisk or cyan) in an ocular motor task. The black line corresponds to the position of the anterior commissure (VCA line). (Reprinted from Nachev P, Rees G, Parton A, Kennard C, Husain M. Volition and conflict in human medial frontal cortex. Curr Biol 15, 122–128, with permission from Elsevier.)

in space), and this in turn must be computed from information about the position of the eye in the orbit, and the direction in which the head and body point. Neurophysiological studies of the parietal lobe have demonstrated populations of neurons with visual responses that are influenced by the direction of gaze, and take into account the direction in which the head points.[90] Such neuronal behavior is a prerequisite for encoding the location of objects in head- and body-centered frames of reference.

How the brain determines the position of the eyes in the head is not settled. The most widely accepted mechanism is that the brain internally monitors its own motor commands (efference copy or corollary discharge),[79,86] and inactivation of pathways from brainstem to cerebral cortex interfere with this mechanism and cause eye movements to become inaccurate.[78] Another possibility is proprioceptive information from the extraocular muscles. Although there appears to be no stretch reflex in the extraocular muscles, proprioceptors do exist in extraocular muscle,[11] and they project to the brainstem via the ophthalmic division of the trigeminal nerve.[61] However, if the trigeminal nerve is cut, eye movement control is not acutely affected, and adaptation to novel visual demands is still possible.[34,48] Other studies sug-

gest that extraocular proprioception may contribute to recovery from extraocular ocular muscle palsy,[47] and could account for suppressive effects of eye muscle surgery on infantile forms of nystagmus.[35] Finally, there is evidence that the brain may also estimate the direction of gaze based upon visual cues. Thus, when normal subjects make saccades to the remembered locations of targets, their eye movements are influenced by the position on a moving visual background at which a target light was previously flashed.[93] Clearly, the brain tries to use every source of information available—efference copy, proprioception, and visual inputs—to determine what might be the correct relation of the eyes and the body to the outside world when these inputs become incongruent as in disease, and symptoms arise.

THE SCIENTIFIC METHOD APPLIED TO THE STUDY OF EYE MOVEMENTS

Our understanding of the way that the brain controls eye movements has advanced conceptually because of the scientific method of formulating and testing hypotheses, an approach championed in this field by D. A. Robinson. Robinson's lecture notes "Linear Control Systems in the Oculomotor System" can be found on the compact disk that accompanies this book. A wealth of information concerning the neural mechanisms for control of eye movements has been provided by electrophysiological and lesion studies in trained monkeys; this information can be readily applied to understanding the effects of human disease by developing testable hypotheses. Conversely, the careful study of patients with disorders of eye movements, with these hypotheses in mind, has led to a better understanding of how the normal brain functions. In this regard, the study of eye movements offers a further advantage because it is relatively easy to construct hypotheses that are quantitative (mathematical models). A most useful approach has been the application of control systems analysis to understanding the effects of feedback and oscillations. A more recent trend has been the application of neural networks to account for the behavior of populations of neurons, with the goal of making more realistic "neu-

romimetic" representations of how the brain works. Such an approach, for example, has been applied to understand better saccadic oscillations such as opsoclonus.[63]

Not all clinicians will want to attempt quantitative mathematical descriptions of disturbed forms of eye movement, but an understanding of certain simple principles of control systems analysis may help in the bedside interpretation of clinical signs. For example, a mismatch of the pulse and step is the cause of the adduction lag encountered in internuclear ophthalmoplegia (see Video Display: Pontine Syndromes). Furthermore, qualitative tests of hypotheses concerning the control of eye movements are often possible using careful clinical observations. Throughout the remaining chapters, we will refer to certain relatively basic principles of control systems analysis that have direct clinical implications.

Finally, the study of eye movements has afforded clinicians a chance to make important contributions to basic neuroscience using bedside observations of eye movement abnormalities in patients from their own clinical practices. Even without fancy instruments or precise quantification, eye movements are so accessible to observation that much is still to be learned at the bedside.

SUMMARY

1. Normal eye movements are a prerequisite for clear, stable, single vision. For best vision of objects such as the words of a book, the images must be brought to the fovea of the retina and held there with image drift less than about 5 degrees per second.

2. Eye movements can be best understood by considering their functions. Of the conjugate types of eye movements, vestibular, optokinetic, and visual fixation systems act to hold images of the seen world steady on the retina; their function is to hold gaze steady. Saccades, smooth pursuit, and vergence eye movements, working together, acquire and hold images of objects of interest on the fovea; their function is to shift gaze. Vergence movements have both gaze-holding and gaze-shifting properties.

3. To move the eyes conjugately (for exam-

ple, as a saccade) requires a phasic-tonic or pulse-step of innervation (Fig. 1–3). The pulse moves the eyes rapidly against viscous forces and the step holds the eyes steady against elastic restoring forces. The pulse is a velocity command; the step is a position command. All eye movement commands have velocity and position components. Position components are created from velocity components by a process of mathematical integration, performed by the nervous system. Fibrous pulleys guide the pulling directions of the extraocular muscles.

4. Vestibular and visually mediated eye movements work together to maintain clear vision during head movements—both rotations (Fig. 1–4) and translations (Fig. 1–5). The vestibulo-ocular reflex promptly produces eye movements to compensate for the brief head perturbations that occur during most natural activities. During sustained head rotations and translations, visually mediated eye movements supplement the vestibular response. If one fixes upon a near object there must also be an adjustment for the translational components of head motion.

5. With the evolution of the fovea and frontal vision, saccadic, smooth pursuit, fixation, and vergence systems became necessary. These gaze-shifting movements are under voluntary control so that it is possible to choose which part of the visual scene one wants to scrutinize using the fovea.

6. The performance of the ocular motor system is undergoing constant recalibration and readjustment to assure optimal visual capabilities. The cerebellum plays an important role in this adaptive control of eye movements.

7. An understanding of the properties of each functional class of eye movements (Table 1–1) will guide the physical examination. Knowledge of the neural substrate of each class of eye movements will aid topological diagnosis. Knowledge of current hypotheses of the control of eye movements aid the interpretation of disorders of ocular motility and may advance understanding of how the brain controls movements of the eyes in normal human beings.

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