40

The Vestibular System

Airplanes and submarines navigate in three dimensions using sophisticated guidance systems that register every acceleration and turn. Laser gyroscopes and computers make these navigational aids extremely precise. Yet the principles of inertial guidance are ancient: Vertebrates have used analogous systems for 500 million years and invertebrates for still longer.

In vertebrates the inertial guidance system is the vestibular system, comprising five sensory organs in the internal ear that measure linear and angular acceleration of the head. Acceleration of the head deflects hair bundles protruding from the hair cells in the inner ear; this distortion changes the cells' membrane potential, altering the synaptic transmission between the cells and the sensory neurons that innervate them. The signals from these vestibular neurons convey information on head velocity and acceleration to vestibular nuclei in the brain stem.

This information keeps the eyes still when the head moves, helps to maintain upright posture, and influences how we perceive our own movement and the space around us by providing a measure of the gravitational field in which we live. In this chapter we describe how the hair cells of the inner ear generate the signals for head acceleration and how these signals are integrated with other sensory information in the brain.

The Vestibular Apparatus in the Inner Ear Contains Five Receptor Organs

Vestibular signals originate in the labyrinths of the internal ear (Figure 40–1). The *bony labyrinth* is a hollow structure within the petrous portion of the temporal

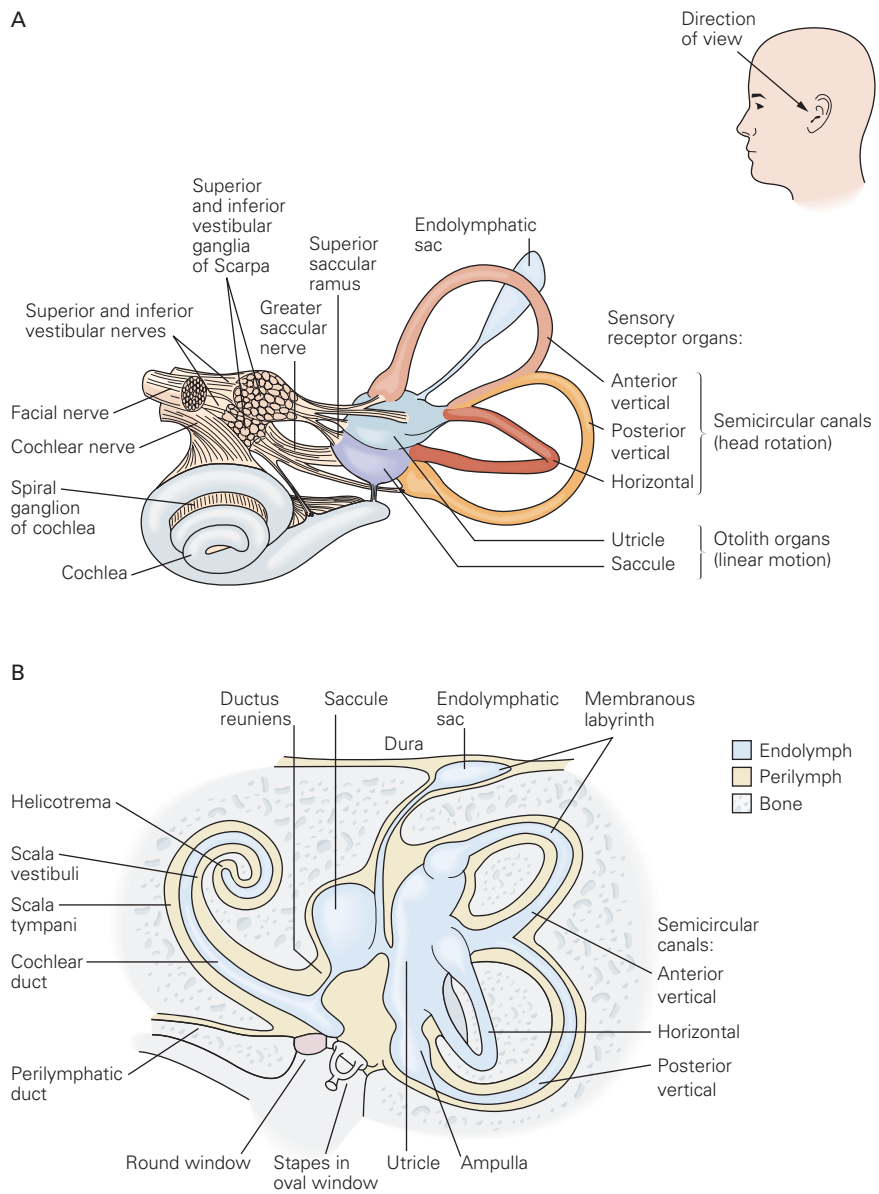

Figure 40–1 The vestibular apparatus of the inner ear.

A. The orientations of the vestibular and cochlear divisions of the inner ear are shown with respect to the head.

B. The inner ear is divided into bony and membranous labyrinths. The bony labyrinth is bounded by the petrous portion of the temporal bone. Lying within this structure is the membranous labyrinth, which contains the receptor organs for hearing (the cochlea) and equilibrium (the utricle, saccule, and semicircular canals). The space between bone and membrane is filled with perilymph, whereas the membranous labyrinth is filled with endolymph. Sensory cells in the utricle, saccule, and ampullae of the semicircular canals respond to motion of the head. (Adapted, with permission, from Iurato 1967.)

bone. Within it lies the *membranous labyrinth,* which contains sensors for both the vestibular and auditory systems.

The membranous labyrinth is filled with *endolymph,* a Na^+-poor, K^+-rich fluid whose composition is maintained by the action of ion pumps in specialized cells. Surrounding the membranous labyrinth, in the space between the membranous labyrinth and the wall of the bony labyrinth, is *perilymph.* Perilymph is a high-Na^+, low-K^+ fluid similar in composition to cerebrospinal fluid, with which it is in communication through the cochlear aqueduct. The endolymph and perilymph are kept separate by a junctional complex that girdles the apex of each cell.

During development the labyrinth progresses from a simple sac to a complex of interconnected sensory organs but retains the same fundamental topological organization. Each organ originates as an epithelium-lined pouch that buds from the otic cyst, and the endolymphatic spaces within the several organs remain continuous in the adult. The endolymphatic spaces of the vestibular labyrinth are also connected to the cochlear duct through the ductus reuniens (Figure 40–1B).

The vestibular portion of the labyrinth, or vestibular apparatus, lies posterior to the cochlea and consists of five sensory structures. Three *semicircular canals* (*horizontal*, also called lateral; *anterior*, also called superior; and *posterior*) sense head rotations, whereas two otolith organs (*utricle* and *saccule*) sense linear motion (also called translation). Because gravity is a linear acceleration, the otolith organs also sense the orientation, or tilt, of the head relative to gravity.

Hair Cells Transduce Mechanical Stimuli into Receptor Potentials

Each of the five receptor organs has a cluster of hair cells responsible for transducing head motion into vestibular signals. Angular or linear acceleration of the head leads to a deflection of the hair bundles in a particular group of hair cells of the appropriate receptor organ (Figure 40–2).

Vestibular signals are carried from the hair cells to the brain stem by branches of the vestibulocochlear nerve (cranial nerve VIII). Cell bodies of the vestibular nerve are located in the vestibular ganglia of Scarpa within the internal auditory canal (Figure 40–1A). The *superior vestibular nerve* innervates the horizontal and anterior canals and the utricle, whereas the *inferior vestibular nerve* innervates the posterior canal and the saccule. The labyrinth's vascular supply, which arises from the anterior inferior cerebellar artery, mirrors its innervation: The anterior vestibular artery supplies the structures innervated by the superior vestibular nerve, and the posterior vestibular artery supplies the structures innervated by the inferior vestibular nerve.

Like most other hair cells, those of the human vestibular system receive efferent inputs from the brain stem. Although the effect of these inputs has not been extensively studied by recording from hair cells in situ, stimulation of the fibers from the brain stem changes the sensitivity of the afferent axons from the hair cells. Stimulation decreases the excitability of some hair cells, as would be expected if activation of the efferent fibers elicited inhibitory postsynaptic potentials in hair cells. In other hair cells, however, activation of the efferent fibers increases excitability.

Given that hair cells are essentially strain gauges (see Chapter 30), the key to grasping how the vestibular organs operate is to understand how mechanical stimuli are delivered to the constituent hair cells. Distinctive mechanical linkages in the otolith organs and semicircular canals account for the contrasting sensitivities of the two types of vestibular organs.

The Semicircular Canals Sense Head Rotation

An object undergoes angular acceleration when its rate of rotation about an axis changes. The head therefore undergoes angular acceleration when it turns or tilts, when the body rotates, and during active or passive locomotion. The three semicircular canals of each vestibular labyrinth detect these angular accelerations and report their magnitudes and orientations to the brain.

Each semicircular canal is a roughly semicircular tube of membranous labyrinth extending from the utricle. One end of each canal is open to the utricle whereas at the other end, the ampulla, the entire lumen of the canal is traversed by a gelatinous diaphragm, the cupula. The cupula is attached to the epithelium along the perimeter and numerous hair bundles insert into the cupula (Figure 40–3).

The vestibular organs detect accelerations of the head because the inertia of their internal contents

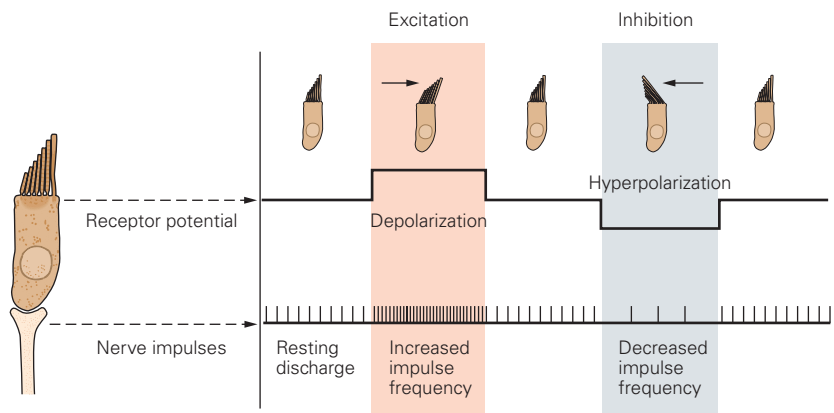

Figure 40–2 Hair cells in the vestibular labyrinth transduce mechanical stimuli into neural signals. At the apex of each cell is a hair bundle, the stereocilia of which increase in length toward a single kinocilium. The membrane potential of the receptor cell depends on the direction in which the hair bundle is bent. Deflection toward the kinocilium causes the cell to depolarize and thus increases the rate of firing in the afferent fiber. Bending away from the kinocilium causes the cell to hyperpolarize, thus decreasing the afferent firing rate. (Adapted, with permission, from Flock 1965.)

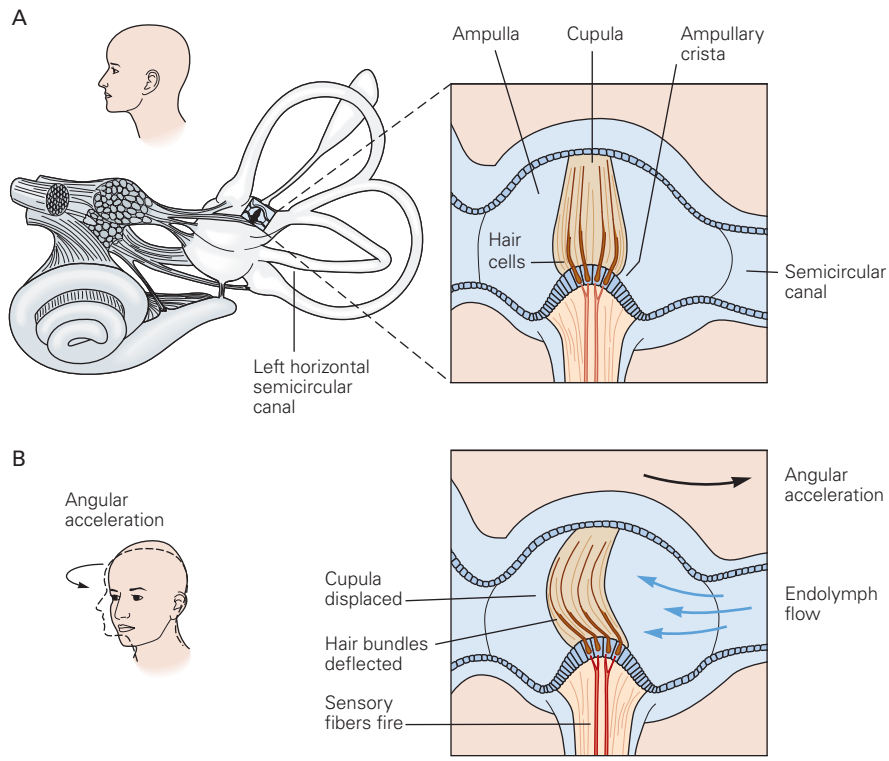

Figure 40–3 The ampulla of a semicircular canal.

A. A thickened zone of epithelium, the ampullary crista, contains the hair cells. The hair bundles of the hair cells extend into a gelatinous diaphragm, the cupula, which stretches from the crista to the roof of the ampulla.

B. The cupula is displaced by the flow of endolymph when the head moves. As a result, the hair bundles are also displaced. Their movement is greatly exaggerated in the diagram.

results in forces on their hair cells. Consider the simplest situation, a rotation in the plane of a semicircular canal. When the head begins to rotate, the membranous and bony labyrinths move along with it. Because of its inertia, however, the endolymph lags behind the surrounding membranous labyrinth, thus rotating within the canal in a direction opposite that of the head.

The motion of endolymph in a semicircular canal can be demonstrated with a cup of coffee. While gently twisting the cup about its vertical axis, observe a particular bubble near the fluid's outer boundary. As the cup begins to turn, the coffee tends to maintain its initial orientation in space and thus counter-rotates in the vessel. If you continue rotating the cup at the same speed, the coffee (and the bubble) eventually catch up to the cup and rotate with it. When the cup decelerates and stops, the coffee keeps rotating, moving in the opposite direction relative to the cup.

In the ampulla this relative motion of the endolymph creates pressure on the cupula, bending it toward or away from the adjacent utricle, depending on the direction of endolymph flow. The resulting deflection of the stereocilia alters the membrane potential of the hair cells, thereby changing the firing rates of the associated sensory fibers. The stereocilia are arranged so that endolymph flow toward the cupula is excitatory for the horizontal canals, whereas flow away from the cupula is excitatory for the anterior and posterior vertical canals.

Each semicircular canal is maximally sensitive to rotations in its plane. The horizontal canal is oriented roughly in the horizontal plane, rising slightly from posterior to anterior, and thus is most sensitive to rotations in the horizontal plane. The anterior and posterior canals are oriented more vertically, approximately 45 degrees from the sagittal plane (Figure 40–4).

Because there is approximate mirror symmetry of the left and right labyrinths, the six canals effectively operate as three coplanar pairs. The two horizontal canals form one pair; each of the other pairs consists of one anterior canal and the contralateral posterior canal. The canal planes are also roughly the pulling planes of the eye muscles. The pair of horizontal canals lies in the pulling plane of the lateral and medial rectus muscles. The left anterior and right posterior pair lies in the pulling plane of the left superior and inferior rectus and right superior and inferior oblique muscles. The right anterior and left posterior pair occupies the pulling plane of the left superior and inferior oblique and right superior and inferior rectus muscles.

The Otolith Organs Sense Linear Accelerations

The vestibular system must compensate not only for head rotations but also for linear motion. The two otolith organs, the utricle and saccule, detect linear motion as well as the static orientation of the head relative to gravity, which is itself a linear acceleration. Each organ consists of a sac of membranous labyrinth approximately 3 mm in the longest dimension. The hair cells of each organ are arranged in a roughly elliptical patch called the *macula.* The human utricle contains approximately 30,000 hair cells, whereas the saccule contains some 16,000.

The hair bundles of the otolithic hair cells extend into a gelatinous sheet, the *otolithic membrane,* that covers the entire macula (Figure 40–5). Embedded on the surface of this membrane are fine, dense particles of calcium carbonate called *otoconia* ("ear dust"), which give the otolith ("ear stone") organs their name. Otoconia are typically 0.5 to 10 µm long; millions of these particles are attached to the otolithic membranes of the utricle and saccule.

Gravity and other linear accelerations exert shear forces on the otoconial matrix and the gelatinous otolithic membrane, which can move relative to the membranous labyrinth. This results in a deflection of the hair bundles, altering activity in the vestibular nerve to signal linear acceleration owing to translational motion or gravity. The orientations of the otolith organs and the directional sensitivity of individual hair cells are such that a linear acceleration along any axis can be sensed. For example, with the head in its normal position, the macula of each utricle is approximately horizontal. Any substantial acceleration in the horizontal plane excites some hair cells in each utricle and inhibits others, according to their orientations (Figure 40–6).

In some instances the vestibular input from a receptor may be ambiguous. For example, acceleration signals from the otolith organs do not distinguish between linear acceleration owing to translation and acceleration owing to gravity (Figure 40–7). The brain, however, integrates inputs from the semicircular canals, otolith organs, and visual and somatosensory systems to properly interpret head and body motions.

The operation of the paired saccules resembles that of the utricles. The hair cells represent all possible orientations within the plane of each macula, but the maculae are oriented vertically in nearly parasagittal planes. The saccules are therefore especially sensitive to vertical accelerations including gravity. Certain saccular hair cells also respond to accelerations in the horizontal plane, in particular those along the anterior–posterior axis.

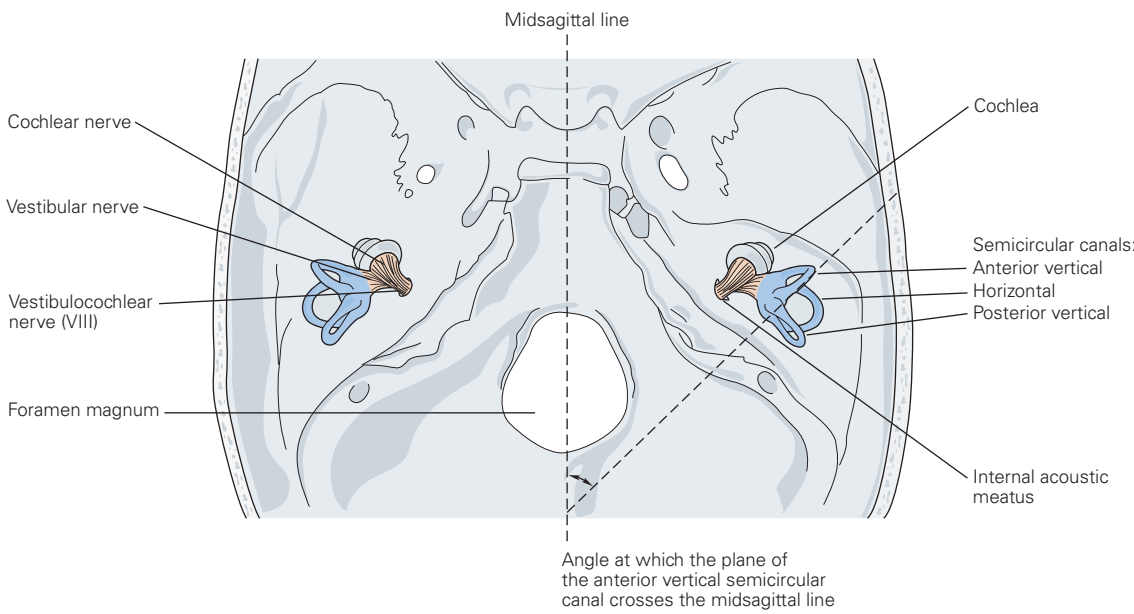

Figure 40–4 The bilateral symmetry of the semicircular canals. The horizontal canals on both sides lie in approximately the same plane and therefore are functional pairs. The bilateral vertical canals have a more complex relationship. The anterior canal on one side and the posterior canal on the opposite side lie in parallel planes and therefore constitute a functional pair.

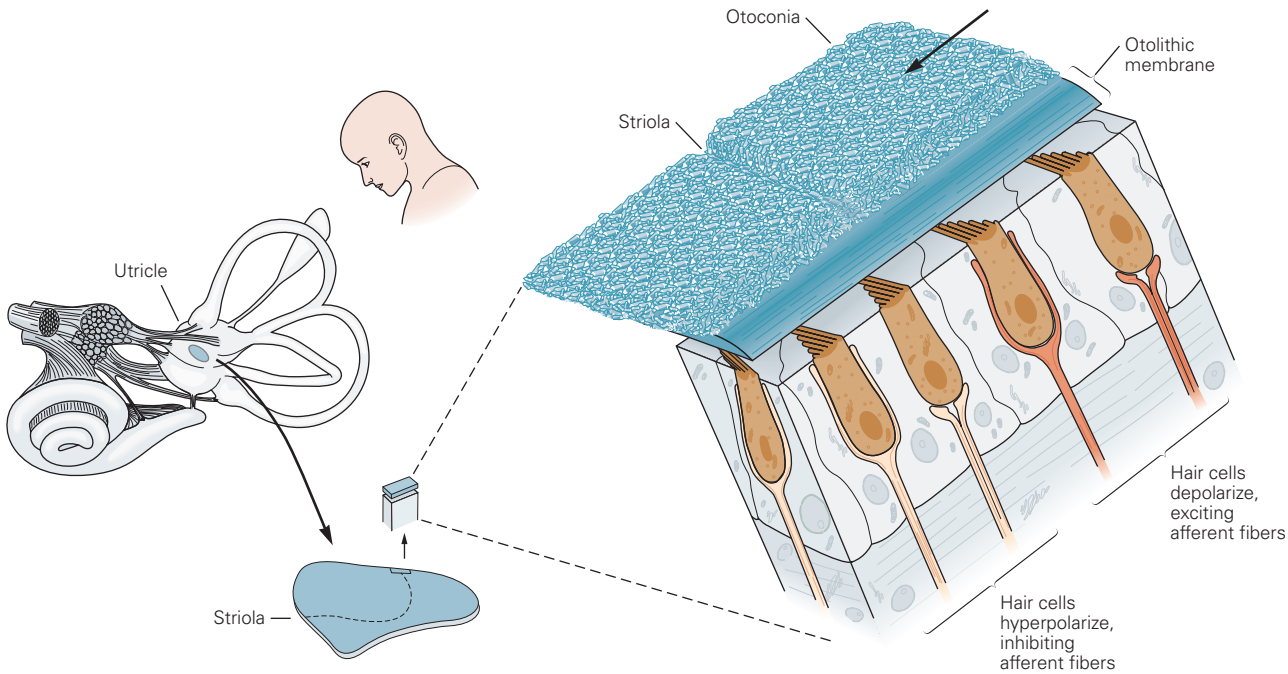

Figure 40–5 The utricle is organized to detect tilt of the head. Hair cells in the epithelium of the utricle have apical hair bundles that project into the otolithic membrane, a gelatinous material that is covered by millions of calcium carbonate particles (otoconia). The hair bundles are polarized but are oriented in different directions (see Figure 40–6). Thus when the head is tilted, the gravitational force on the otoconia bends each hair bundle in a particular direction. When the head is tilted in the direction of a hair cell's axis of polarity, that cell depolarizes and excites the afferent fiber. When the head is tilted in the opposite direction, the same cell hyperpolarizes and inhibits the afferent fiber. (Adapted, with permission, from Iurato 1967.)

Most Movements Elicit Complex Patterns of Vestibular Stimulation

Although the actions of the vestibular organs may be separated conceptually and experimentally, actual human movements generally elicit a complex pattern of excitation and inhibition in several receptor organs in both labyrinths. Consider, for example, the act of leaving the driver's seat of an automobile.

As you begin to swivel toward the door, both horizontal semicircular canals are stimulated strongly. The simultaneous lateral movement out the car's door stimulates hair cells in both utricles in a pattern that changes continuously as the orientation of the turning head changes with respect to the direction of bodily movement. When rising to a standing position, the vertical acceleration excites an appropriately oriented complement of hair cells in each of the saccules while inhibiting an oppositely oriented group. Finally, the maneuver's conclusion involves linear and angular accelerations opposite to those when you started to leave the car.

Vestibulo-Ocular Reflexes Stabilize the Eyes and Body When the Head Moves

The vestibular nerve transmits information about head acceleration to the vestibular nuclei in the medulla, which then distribute it to higher centers. This central network of vestibular connections is responsible for the vestibulo-ocular reflexes that the body uses to compensate for head movement. These neurons also determine the perception of the body's motion in space. Vestibular signals also enable the skeletal motor system to compensate for head movement. The vestibulospinal reflexes are discussed in Chapter 41.

Stable images on the retina are perceived better than moving ones. When the head moves, the eyes are kept still by the vestibulo-ocular reflexes. If you shake your head while reading you can still discern words because of the vestibulo-ocular reflexes. If instead you move the book at a similar speed, however, you can no longer read the words. In the latter instance vision is the brain's only cue for stabilization of the image

on the retina, and visual processing is much slower and less effective than vestibular processing for image stabilization. The vestibular apparatus signals how fast the head is rotating, and the oculomotor system uses this information to stabilize the eyes to fix visual images on the retina.

There are three different vestibulo-ocular reflexes. The *rotational vestibulo-ocular reflex* compensates for head rotation and receives its input predominantly from the semicircular canals. The *translational vestibulo-ocular reflex* compensates for linear head movement. The *ocular counter-rolling response* compensates for head tilt in the vertical plane.

The Rotational Vestibulo-Ocular Reflex Compensates for Head Rotation

When the semicircular canals sense head rotation in one direction, the eyes usually begin to rotate in the opposite direction in the orbits. Ideally, eye velocity is matched to head velocity, minimizing retinal motion. This compensatory eye rotation is called the *vestibular slow phase,* although it is not necessarily slow: The eyes may reach speeds of more than 200 degrees per second if the head's rotation is fast. With continued head rotation the eyes would eventually reach the limit of their orbital range and stop moving. To prevent this, a rapid saccade-like movement called a *quick phase* displaces the eyes to a new point of fixation in the direction of head rotation.

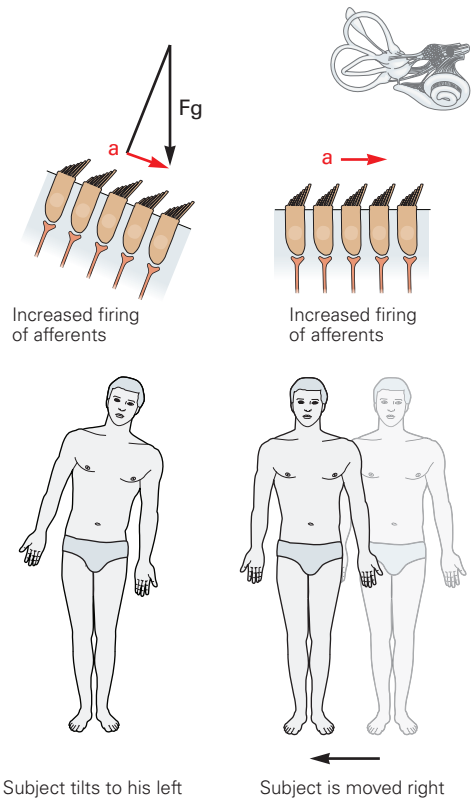

Figure 40–7 **Vestibular inputs signalling body posture and motion can be ambiguous.** The postural system cannot distinguish between tilt and linear acceleration of the body based on otolithic inputs alone. The same shearing force acting on vestibular hair cells can result from tilting of the head (**left**), which exposes the hair cells to a portion of the acceleration (**a**) owing to gravity (**Fg**), or from horizontal linear acceleration of the body (**right**).

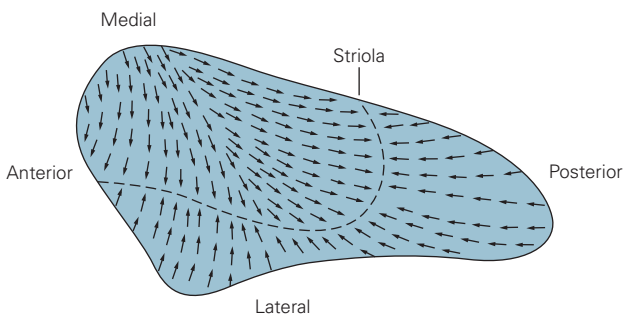

Figure 40–6 **The axis of mechanical sensitivity of each hair cell in the utricle is oriented toward the striola.** The striola curves across the surface of the macula, resulting in a characteristic variation in the axes of mechanosensitivity (**arrows**) in the population of hair cells. Because of this arrangement, tilt in any direction depolarizes some cells and hyperpolarizes others, while having no effect on the remainder. (Adapted, with permission, from Spoendlin 1966.)

If rotation is prolonged, the eyes execute alternating slow and quick phases called *nystagmus* (Greek *nod*), so called because a nod has a slow phase as the head drops and a quick phase as the head snaps back to an erect position (Figure 40–8). Although the slow phase is the primary response of the rotational vestibulo-ocular reflex, the direction of nystagmus is defined in clinical practice by the direction of its quick phase. Thus, rightward rotation excites the right horizontal canal and inhibits the left horizontal canal. This leads to leftward slow phases and a *right-beating nystagmus.*

If the angular velocity of the head remains constant, the inertia of the endolymph is eventually overcome, as in the coffee cup example earlier: The cupula relaxes and vestibular nerve discharge returns to its

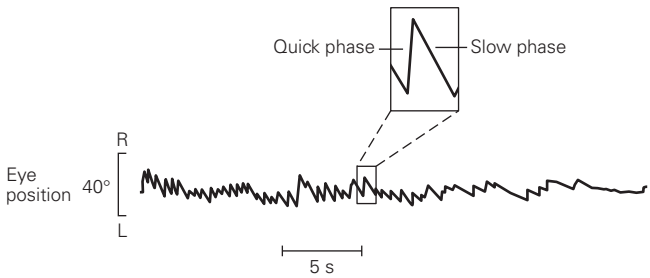

Figure 40–8 Vestibular nystagmus. The trace shows the eye position of a subject in a chair rotated counterclockwise at a constant rate in the dark. At the beginning of the trace the eye moves slowly at the same speed as the chair (slow phase) and occasionally makes rapid resetting movements (quick phase). The speed of the slow phase gradually decreases until the eye no longer moves regularly. (Reproduced, with permission, from Leigh and Zee 1991.)

baseline rate. As a consequence, slow-phase velocity decays and the nystagmus stops, although the head is still rotating.

In fact, the nystagmus lasts longer than would be expected based on cupular deflection. By a process called *velocity storage*, a brain stem network provides a velocity signal to the oculomotor system, although the vestibular nerve no longer signals head movement. Eventually, however, the nystagmus does decay and the sense of motion vanishes.

If head rotation stops abruptly, the endolymph continues to move in the same direction that the head had formerly rotated. With rightward rotation this inhibits the right horizontal canal and excites the left horizontal canal, resulting in a sensation of leftward rotation and a corresponding left-beating nystagmus. However, this occurs only in darkness. In the light, optokinetic reflexes maintain nystagmus as vestibular input diminishes, as long as the head continues to rotate. Correspondingly, optokinetic reflexes suppress post-rotatory nystagmus in the light.

The Otolithic Reflexes Compensate for Linear Motion and Head Deviations

The semicircular canals detect only head rotation; linear motion is sensed by the otolith organs. Linear movement presents the vestibular system with a more complex geometrical problem than does rotation.

When the head rotates, all images move with the same velocity on the retina. When the head moves sideways, however, the image of a close object moves more rapidly across the retina than does the image of a distant object. This can be understood easily by considering what happens when a person looks out the side window of a moving car: Objects near the side of the road move out of view almost with the speed of the car, whereas distant objects disappear more slowly. To compensate for linear head movement the vestibular system must take into account the distance to the object being viewed—the more distant the object, the smaller the eye movement.

Because gravity exerts a constant linear acceleration force on the head, the otolith organs also sense the orientation of the head relative to gravity. When the head tilts away from the vertical in the roll plane—around the axis running from the occiput to the nose—the eyes rotate in the opposite direction, along the axis of torsion, to reduce the tilt of the retinal image. This torsional eye rotation in response to head tilt is the ocular counter-rolling reflex.

Vestibulo-Ocular Reflexes Are Supplemented by Optokinetic Responses

The vestibulo-ocular reflexes represent movement imperfectly. They are best at sensing the onset or abrupt change of motion; they compensate poorly for sustained motion at constant speed during translation or constant angular velocity during rotation. In addition, they are insensitive to very slow rotations or linear accelerations.

Thus vestibular responses during prolonged motion in the light are supplemented by two visual following reflexes that maintain nystagmus when there is no longer any vestibular input. *Optokinetic nystagmus* refers to the response to full-field visual motion; *pursuit* involves the fovea following a small target. Although the two reflexes are distinct, their pathways overlap.

Central Connections of the Vestibular Apparatus Integrate Vestibular, Visual, and Motor Signals

The Vestibular Nerve Carries Information on Head Velocity to the Vestibular Nuclei

When the head is at rest there is a spontaneous tonic discharge in the bilateral vestibular nerves that is equal on both sides. That there is no imbalance in the firing rates indicates to the brain that the head is not moving. When the head rotates, the horizontal canal toward which the head is turning is excited whereas the opposite canal is inhibited, resulting in phasic increases and

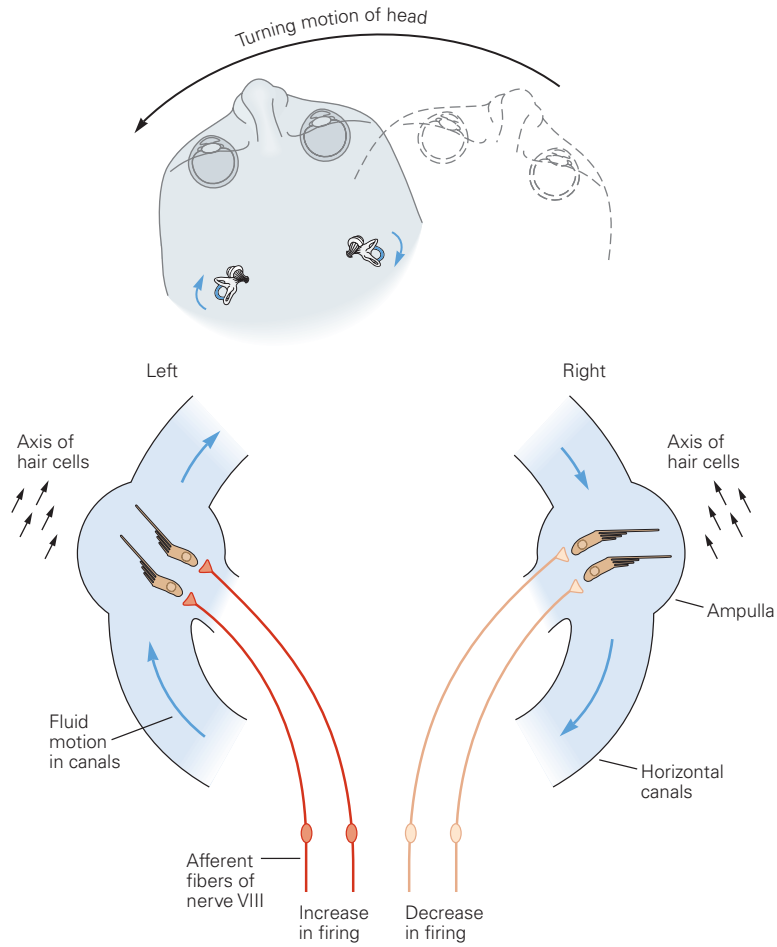

Figure 40–9 The left and right horizontal semicircular canals work together to signal head movement. Because of inertia, rotation of the head in a counterclockwise direction causes endolymph to move clockwise with respect to the canals. This deflects the stereocilia in the left canal in the excitatory direction, thereby exciting the afferent fibers on this side. In the right canal the afferent fibers are hyperpolarized so that firing decreases.

decreases in the vestibular signal (Figure 40–9). The phasic signal correlates with head velocity.

The vestibular nerve projects ipsilaterally from the vestibular ganglion to four *vestibular nuclei* in the dorsal part of the pons and medulla, in the floor of the fourth ventricle. These nuclei integrate signals from the vestibular organs with signals from the spinal cord, cerebellum, and visual system. They project in turn to several central targets: the oculomotor nuclei, reticular and spinal centers concerned with skeletal movement, the vestibular regions of the cerebellum (flocculus, nodulus, ventral paraflocculus, and ventral uvula), and the thalamus. In addition, each vestibular nucleus projects to other vestibular nuclei, both ipsilateral and contralateral.

The vestibular nuclei—medial, lateral, superior, and descending—were originally distinguished by their cytoarchitecture. Their anatomical differences correspond approximately to functional differences (Figure 40–10).

The superior and medial vestibular nuclei receive fibers predominantly from the semicircular canals. They send fibers to oculomotor centers and to the spinal cord. Neurons in the medial vestibular nucleus are predominantly excitatory, whereas those in the superior vestibular nucleus are chiefly inhibitory. These nuclei are concerned primarily with reflexes that control gaze (see Chapter 39).

The lateral vestibular nucleus (Deiters' nucleus) receives fibers from the semicircular canals and otolith organs and projects mostly into the lateral vestibulospinal tract. This nucleus is concerned principally with postural reflexes. The descending vestibular nucleus receives predominantly otolithic input and projects to the cerebellum and reticular formation as well as to the contralateral vestibular nuclei and the spinal cord. This nucleus is thought to be involved in integrating vestibular signals with central motor information. Vestibular projections to the spinal systems are discussed in Chapter 41.

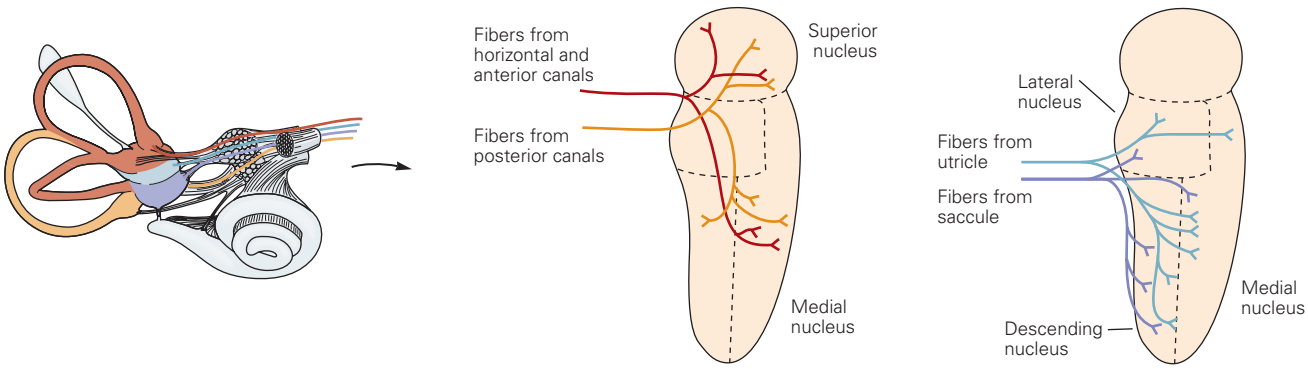

Figure 40–10 Sensory inputs to the vestibular nuclei. Neurons in the superior and medial vestibular nuclei receive input predominantly from the semicircular canals but also from the otolith organs. Neurons in the lateral vestibular nucleus (Deiters' nucleus) receive input from the semicircular canals and otolith organs. This nucleus is concerned predominantly with postural reflexes. The descending vestibular nucleus receives input predominantly from the otolith organs. (Adapted, with permission, from Gacek and Lyon 1974.)

A Brain Stem Network Connects the Vestibular System with the Oculomotor System

During fast head movements the vestibulo-ocular reflex must act quickly to maintain stable gaze. A disynaptic brain stem pathway, the three-neuron arc, connects each semicircular canal to the appropriate eye muscle (Figure 40–11). A direct pathway for the horizontal vestibulo-ocular reflex, the ascending tract of Deiters, is anatomically significant but may not be physiologically important. Even when Deiters' tract is intact, lesions of the medial longitudinal fasciculus impair the contribution of the medial rectus muscle to the horizontal vestibulo-ocular reflex.

The oculomotor centers for vertical and torsional movements lie in the mesencephalic reticular formation (see Chapter 39). Networks similar to those for the horizontal canals connect the vertical canals to their oculomotor targets.

These excitatory and inhibitory pathways of the vestibulo-ocular reflex connect each of the three pairs of semicircular canals to the four extraocular muscles, two for each eye, whose pulling directions are in roughly the same plane. For example, a leftward and downward head motion, such as tilting the head toward the front of the left shoulder, excites the left anterior canal and inhibits the right posterior canal. In turn, the left anterior canal excites the left superior rectus and right inferior oblique muscles, which move the eyes upward and to the right, and inhibits the left inferior rectus and right superior oblique muscles, which move the eyes downward and to the left. Simultaneously, the inhibited right posterior canal decreases its excitation of the left inferior rectus and right superior oblique, which move the eyes downward and to the left, and decreases its inhibition of the left superior rectus and right inferior oblique, which move the eyes upward and to the left. The primary muscle targets of the three canals are listed in Table 40–1.

Less is known of the central pathways mediating otolithic reflexes (translational vestibulo-ocular reflexes). Patients with cerebellar disease often have diminished vestibulo-ocular responses to linear motion but not rotation of the head, suggesting that the cerebellum is essential for the translational vestibulo-ocular reflexes.

Two Visual Pathways Drive the Optokinetic Reflexes

As we have seen, movement of images on the retina or head movement can induce nystagmus and the perception of self-motion. This perception occurs because vision-related neurons project to the vestibular nuclei. Retinal neurons project to the accessory optic system and the nucleus of the optic tract in the pretectum, which project to the same medial vestibular nucleus that receives signals from vestibular organs. Vestibular neurons that receive this visual input cannot distinguish between visual and vestibular signals (Figure 40–12). They respond identically to head movement and to motion of an image across the retina, which is presumably why people sometimes cannot distinguish the two.

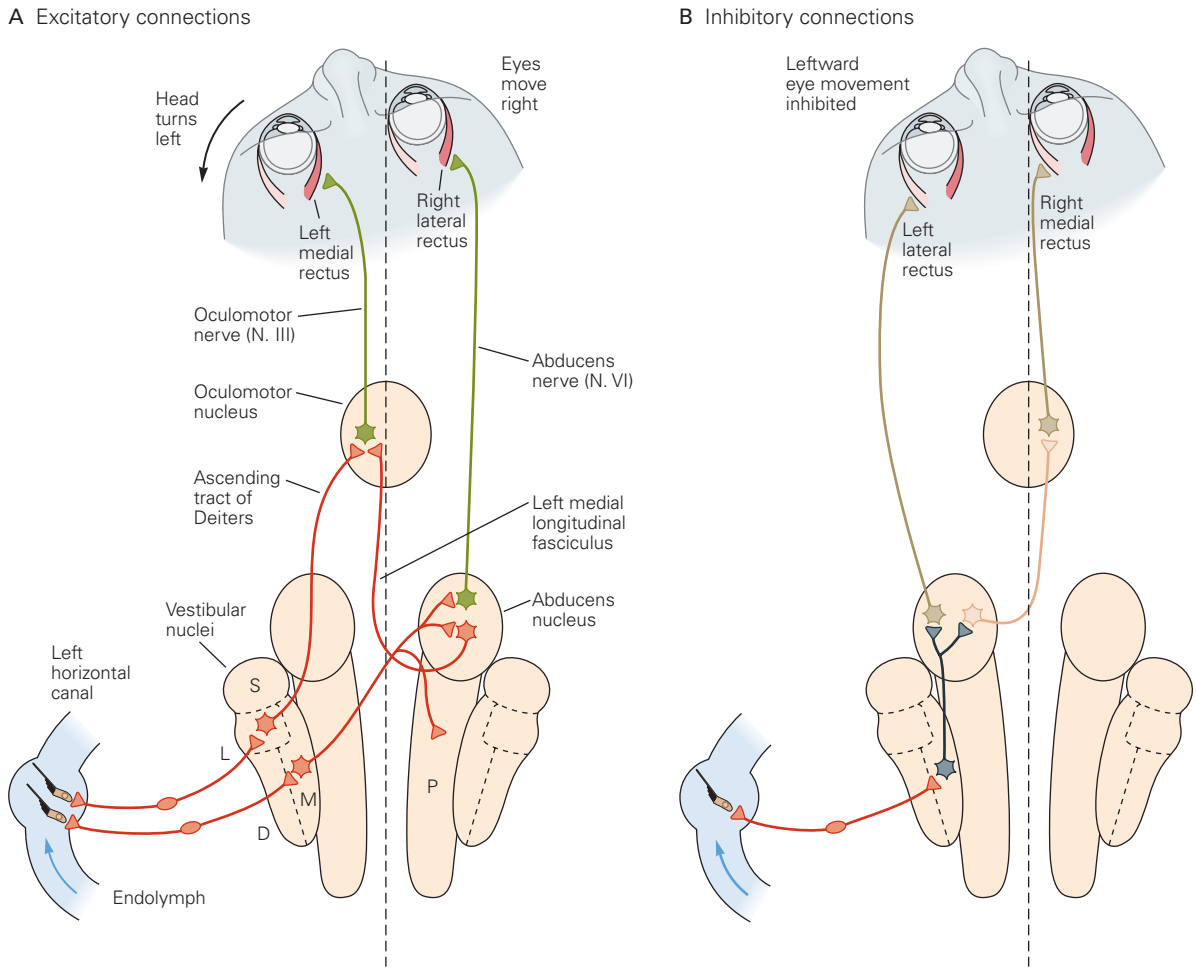

Figure 40–11 The horizontal vestibulo-ocular reflex. Similar pathways connect the anterior and posterior canals to the vertical recti and oblique muscles.

A. Leftward head rotation excites hair cells in the left horizontal canal, thus exciting neurons that evoke rightward eye movement. The vestibular nuclei include two populations of first-order neurons. One lies in the medial vestibular nucleus (**M**); its axons cross the midline and excite neurons in the right abducens nucleus and nucleus prepositus hypoglossi (**P**). The other population is in the lateral vestibular nucleus (**L**); its axons ascend ipsilaterally in the tract of Deiters and excite neurons in the left oculomotor nucleus, which project in the oculomotor nerve to the left medial rectus muscle.

The right abducens nucleus has two populations of neurons. A set of motor neurons projects in the abducens nerve and excites the right lateral rectus muscle. The axons of a set of interneurons cross the midline and ascend in the left medial longitudinal fasciculus to the oculomotor nucleus, where they excite the neurons that project to the left medial rectus muscle. These connections facilitate the rightward horizontal eye movement that compensates for leftward head movement. Other nuclei shown are the superior (**S**) and descending (**D**) vestibular nuclei.

B. During counterclockwise head movement, leftward eye movement is inhibited by sensory fibers from the left horizontal canal. These afferent fibers excite neurons in the medial vestibular nucleus that inhibit motor neurons and interneurons in the left abducens nucleus. This action reduces the excitation of the motor neurons for the left lateral and right medial rectus muscles. The same head movement results in a decreased signal in the right horizontal canal (not shown), which has similar connections. The weakened signal results in decreased inhibition of the right lateral and left medial rectus muscles and decreased excitation of the left lateral and right medial rectus muscles. (Adapted, with permission, from Suguichi et al. 2005.)

Table 40–1 Primary Muscle Targets of the Semicircular Canals

Canal	Ipsilateral muscles	Contralateral muscles
Horizontal	Excite medial rectus Inhibit lateral rectus	Excite lateral rectus Inhibit medial rectus
Anterior	Excite superior rectus Inhibit inferior rectus	Excite inferior oblique Inhibit superior oblique
Posterior	Excite superior oblique Inhibit inferior oblique	Excite inferior rectus Inhibit superior rectus

In rabbits, which are lateral-eyed and afoveate, optokinetic reflexes depend primarily on brain stem pathways involving the pretectal visual system. The rabbit optokinetic response is stronger when the image moves in a temporal-to-nasal direction and is relatively more efficient at low image speeds. The same asymmetry is seen in human infants and in patients with certain abnormalities of visual development, such as hereditary achromatopsia. Such asymmetries disappear in adult humans and nonhuman primates, which have well-developed binocular vision and thus a powerful cortical projection to the pretectum.

The Cerebral Cortex Integrates Vestibular, Visual, and Somatosensory Inputs

All vestibular nuclei project to the ventral posterior and ventral lateral nuclei of the thalamus, which then project to two regions in the primary somatosensory cortex (S-I): the vestibular regions of areas 2 and 3a (Figure 40–13). Vernon Mountcastle first showed that electrical stimulation of the vestibular nerve in the cat evoked activity in the primary somatosensory cortex (S-I) and in a parietal association cortex (area 7). Otto-Joachim Grüsser described neurons in areas 2 and 3a of the monkey that respond to head rotation. Vestibular activity has also been found in the monkey in the parieto-insular vestibular cortex, which is near the secondary somatosensory area (S-II), and in the periarcuate regions of the frontal lobe.

Single-cell recordings in animals have shown that these areas receive not only vestibular but also visual and somatosensory inputs. This arrangement likely

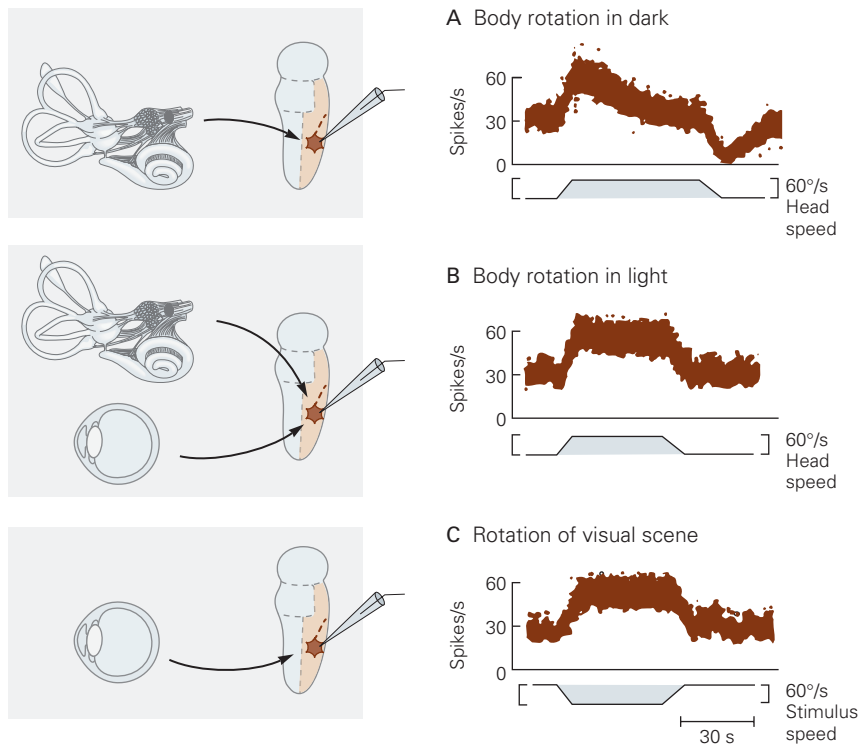

Figure 40–12 Individual neurons in the medial vestibular nucleus of a monkey receive both visual and vestibular signals. Each panel shows the spike rate of a single neuron over time. The angular velocity of the turntable used to rotate the subject or visual scene is shown below the plot. (Adapted, with permission, from Waespe and Henn 1977.)

A. When the animal is rotated in the dark, the activity of the neuron gradually falls to the baseline even while the animal is still rotating.

B. When the animal is rotated in the light, the discharge is maintained throughout rotation.

C. When the animal is still while the visual scene rotates around it, the neuron in the steady state responds as if the animal were rotating in the light, although it takes somewhat longer for the neuron to reach a constant level of activity. The similarity of response between body rotation in the light and rotation of the visual scene may explain why people sometimes feel they are moving when in fact the visual scene is moving.

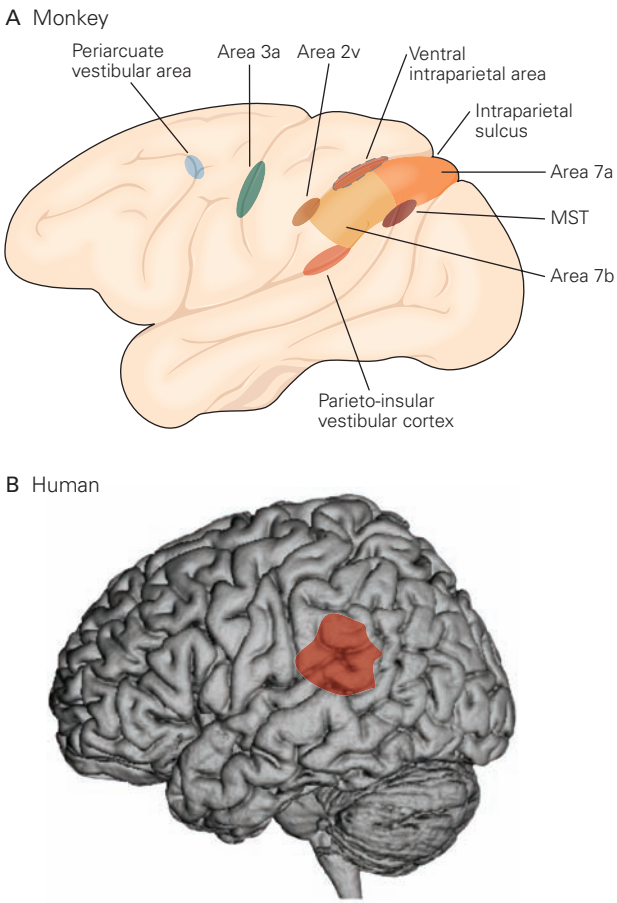

Figure 40–13 The vestibular cortex.

A. This lateral view of a monkey's brain shows the areas of cerebral cortex in which vestibular responses have been recorded. (MST, medial superior temporal area.)

B. Areas of human cortex that respond selectively to galvanic stimulation of the vestibular system. (Adapted, with permission, from Brandt and Dietrich 1999.)

facilitates the integration of all relevant sensory information for the perception of motion and orientation. In addition, vestibular and visual areas of cortex have reciprocal connections that may be involved in the resolution of contradictory vestibular and visual inputs. For example, motion of an object in the visual field of a person riding in a train or car moving at constant speed is correctly interpreted as self-motion, even though there is no corresponding vestibular signal. An undesired consequence of this is that motion in the visual field is often interpreted as self-motion even when a person is not moving, as when the observer has stopped at a red light and the adjacent vehicle accelerates.

Although the vestibular apparatus measures how one accelerates and tilts, the cerebral cortex employs this information to generate a subjective measure of self-movement in relation to the external world. Otolithic inputs are used by the vestibular cortex to determine the gravitational vertical axis in the visual field. Patients with lesions in this area may perceive themselves or objects in the environment to be tilted away from the side of the lesion. A few patients with parietal lesions perceive their visual environments to be rotated by 90 or 180 degrees.

The Cerebellum Adjusts the Vestibulo-Ocular Reflex

As we have seen, the vestibulo-ocular reflex keeps the gaze constant when the head moves. There are times, however, when the reflex is inappropriate. For example, when you turn your head while walking, you want your gaze to follow; the rotational vestibulo-ocular reflex, however, would prevent your eyes from turning with your head. To prevent this sort of biologically inappropriate response, the reflex is under the control of the cerebellum, which permits visual suppression of the vestibulo-ocular reflex.

In addition, the vestibulo-ocular reflex must be continuously calibrated to maintain its accuracy in the face of changes within the motor system (fatigue, injury to vestibular organs or pathways, eye-muscle weakness, or aging) and differing visual requirements (wearing corrective lenses). This is accomplished by sensory feedback that modifies the motor output. If the reflex is not working properly, the image moves across the retina. The motor command to the eye muscles must be adjusted until the gaze is again stable, retinal image motion is zero, and there is no error.

Anyone who wears eyeglasses depends on this plasticity of the vestibulo-ocular reflex. Because lenses for nearsightedness shrink the visual image, a smaller eye rotation is needed to compensate for a given head rotation, and the gain of the vestibulo-ocular reflex must be reduced. Conversely, glasses for farsightedness magnify the image, so the vestibulo-ocular reflex gain must increase during their use. More complicated is the instance of bifocal spectacles, in which the vestibulo-ocular reflex must use different gains for the two lenses. In the laboratory the vestibulo-ocular reflex can be conditioned by altering the visual consequences of head motion. For example, if a subject is rotated for a period of time while wearing magnifying glasses, the vestibulo-ocular reflex gain gradually increases (Figure 40–14A).

This process requires changes in synaptic transmission in both the cerebellum and the brain stem.

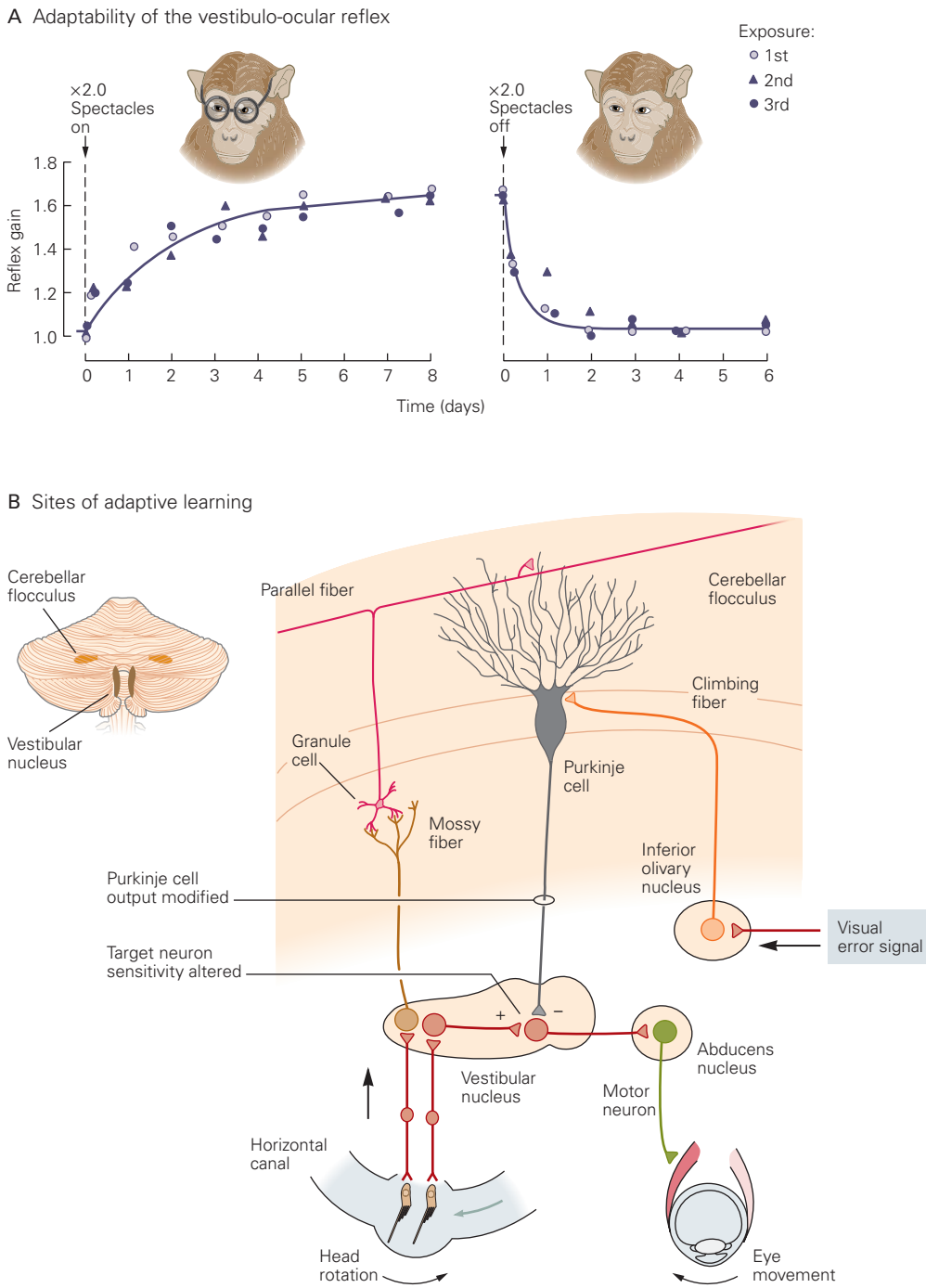

Figure 40–14 The vestibulo-ocular reflex is adaptable.

A. For several days the monkey continuously wears magnifying spectacles that double the speed of the retinal-image motion evoked by head movement. Each day the gain of the vestibulo-ocular reflex—the amount the eyes move for a given head movement—is tested in the dark so that the monkey cannot use retinal motion as a clue to modify the reflex. Over a period of 4 days the gain increases gradually (**left**). It quickly returns to normal when the spectacles are removed (**right**). (Adapted, with permission, from Miles and Eighmy 1980.)

B. Adaptation of the vestibulo-ocular reflex occurs in cerebellar and brain stem circuits. A visual error signal, triggered by motion of the retinal image during head movement, reaches the inferior olivary nucleus. The climbing fiber transmits this error signal to the Purkinje cell, affecting the parallel fiber–Purkinje cell synapse. The Purkinje cell transmits changed information to the floccular target cell in the vestibular nucleus, changing its sensitivity to the vestibular input. After the reflex has been adapted, the Purkinje cell input is no longer necessary.

If the flocculus and paraflocculus of the cerebellum are lesioned, the gain of the vestibulo-ocular reflex can no longer be modulated. Mossy fibers carry vestibular, visual, and motor signals from the pontine nuclei to the cerebellar cortex; the granule cells, with their parallel-fiber axons, relay these signals to the Purkinje cells (Figure 40–14B). David Marr suggested that the synaptic efficacy of parallel fiber input to a Purkinje cell could be modified by the concurrent action of climbing fiber input. Masao Ito showed that the climbing fiber input to the cerebellum did indeed carry a suitable visual error signal and postulated that this was the "teaching line" enabling the cerebellum to correct the error in the vestibulo-ocular reflex. This adaptation requires long-term depression of the Purkinje cell synapses (see Chapter 42). Transgenic mice lacking long-term synaptic depression in these neurons cannot adapt their vestibulo-ocular reflexes in a few hours, as can normal mice.

The Purkinje cell is not the only locus of change. Frederick Miles and Steven Lisberger showed that there is a class of neurons in the vestibular nucleus, the *flocculus target neurons,* that receive GABA-ergic inhibitory input from Purkinje cells in the flocculus as well as direct inputs from vestibular sensory fibers. During adaptation of the vestibulo-ocular reflex these neurons change their sensitivity to the vestibular inputs in the appropriate way, and after adaptation they can maintain those changes without further input from the cerebellum.

The importance of the cerebellum in calibrating eye movements is also evident in patients with cerebellar disease. Although the vestibulo-ocular reflex is still present, it may have an abnormal amplitude or direction. In many cases the translational vestibulo-ocular reflex is also poor.

Clinical Syndromes Elucidate Normal Vestibular Function

Unilateral Vestibular Hypofunction Causes Pathological Nystagmus

As we have seen, rotation excites hair cells in the semicircular canal whose hair bundles are oriented in the direction of motion and inhibits those whose hair bundles are oriented away from the motion. This imbalance in vestibular signals is responsible for the compensatory eye movements and the sensation of rotation that accompanies head movement. It can also originate from disease of one labyrinth or vestibular nerve, which results in a pattern of afferent vestibular signaling analogous to that stemming from rotation away from the side of the lesion, that is, more discharge from the intact side. There is accordingly a strong feeling of spinning, called vertigo.

The vestibulo-ocular reflex responds by generating eye movements in an attempt to compensate for this perceived rotation. The slow phases (see Figure 40–8) are directed away from the intact side and toward the lesioned side, and the intervening quick phases produce a nystagmus that beats toward the intact side. For example, an acute loss of left vestibular function causes a right-beating nystagmus, as if there were a prolonged rightward acceleration. Unlike physiological nystagmus, which stabilizes gaze, the pathological nystagmus causes retinal slip and a corresponding sensation that the visual world is moving, called *oscillopsia.*

The vertigo and nystagmus resulting from an acute vestibular lesion typically subside over several days, even if peripheral function does not recover. First, nystagmus can be suppressed by visual fixation, just as post-rotatory nystagmus is suppressed in the light. Second, central compensatory mechanisms restore the balance in vestibular signals in the brain stem, even when peripheral input is permanently lost.

The loss of input from one labyrinth also means that all vestibular reflexes must be driven by a single labyrinth. For the vestibulo-ocular reflex this condition is quite effective at low speeds because the intact labyrinth can be both excited and inhibited. However, during rapid, high-frequency rotations inhibition is not sufficient, such that the gain of the reflex is reduced when the head rotates toward the lesioned side. This is the basis of an important clinical test of canal function, the head-impulse test. In this test the head is moved rapidly one time along the axis of rotation of a single canal. If there is a significant decrease in gain owing to canal dysfunction, the movement of the eyes will lag behind that of the head, and there will be a visible catch-up saccade (Figure 40–15).

Bilateral Vestibular Hypofunction Interferes with Normal Vision

Vestibular function is sometimes lost simultaneously on both sides, for example from ototoxicity owing to aminoglycoside antibiotics such as gentamicin. The symptoms of bilateral vestibular hypofunction are different from those of unilateral loss. First, there is no vertigo because there is no imbalance in vestibular signals; input is reduced equally from both sides. For the same reason there is no spontaneous nystagmus. In fact, these patients may have no symptoms when they are at rest and the head is still.

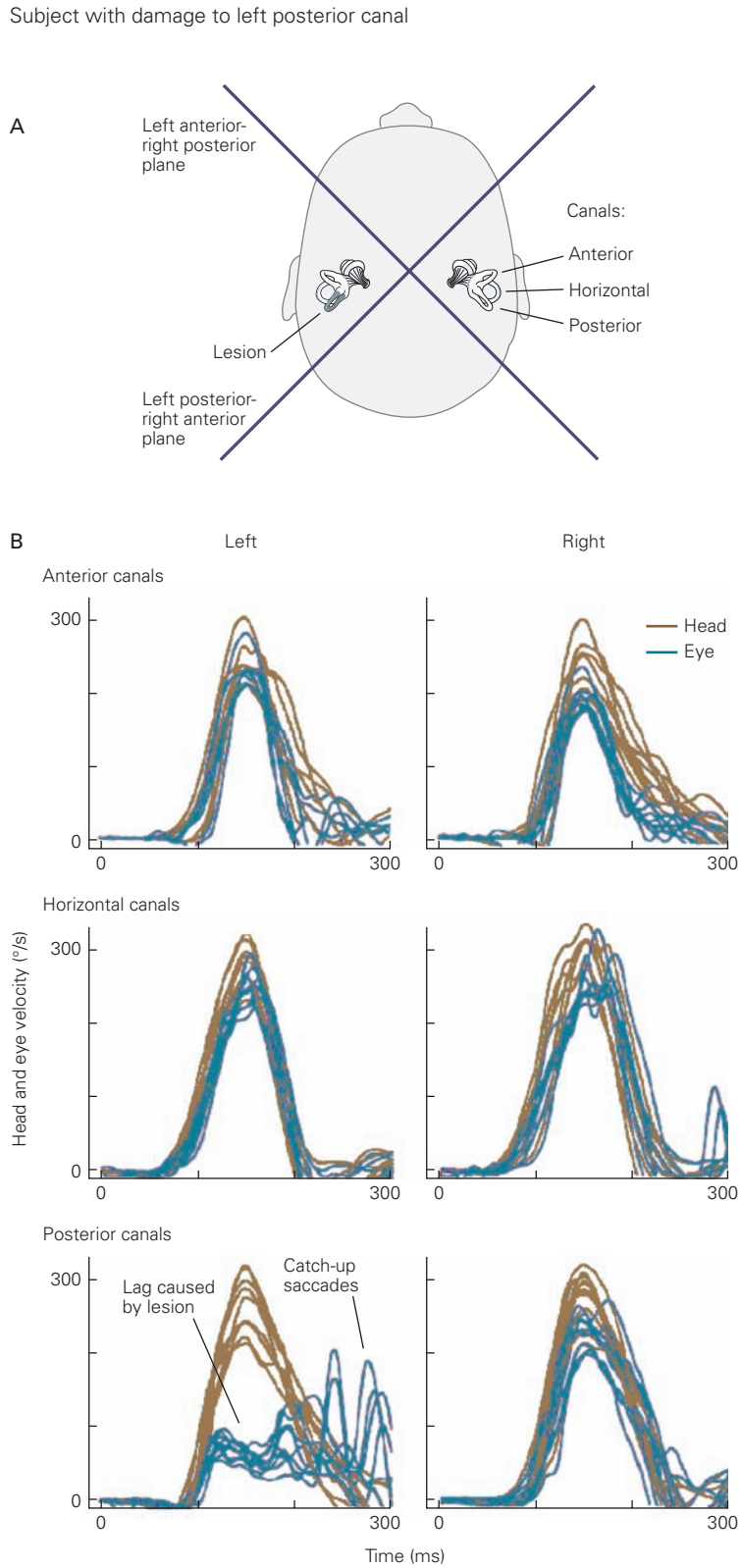

Figure 40–15 Clinical testing of the vestibulo-ocular reflex.

A. The examiner rotates the patient's head rapidly in the optimum direction for each canal while the subject fixates. This stimulus is termed a *head impulse*. If the canal and oculomotor systems are normal, eye velocity matches head velocity and the eyes maintain gaze—they do not move relative to the external environment. If there is a canal deficit, the eyes lag behind the head and make catch-up saccades after the head movement is finished.

B. The records are the results of impulse testing in a patient with a lesion of the left posterior canal. In the record for the left posterior canal (rotation in the left posterior–right anterior plane), eye velocity fails to track the head velocity during the most rapid parts of the head movement. After the head movement is over, pulses of eye velocity correspond to the catch-up saccades induced by the visual error.

Nevertheless, the loss of vestibular reflexes is devastating. A physician who lost his vestibular hair cells because of a toxic reaction to streptomycin wrote a dramatic account of this loss. Immediately after the onset of streptomycin toxicity he could not read in bed without steadying his head to keep it motionless. Even after partial recovery he could not read street signs or recognize friends while walking in the street; he had to stop to see clearly. Some patients may even "see" their heartbeat if the vestibulo-ocular reflex fails to compensate for the miniscule head movements that accompany each arterial pulse.

An Overall View

The vestibular system evolved to answer two of the questions basic to human life: "Which way is up?" and "Where am I going?" The system provides the brain with a rapid estimate of head motion. Although this estimate could be derived from vision and neck proprioception, those sensory mechanisms are slow and cumbersome. In contrast, the hair cells of the vestibular system sense head acceleration directly, and this responsiveness in turn allows those reflexes that require information about head motion to act efficiently and quickly.

There are two distinct sets of vestibular organs. The three semicircular canals sense head rotation, whereas the otolith organs—the utricle and saccule—detect linear acceleration. Signals from the canals and otolith organs are carried in the vestibular nerve to the ipsilateral vestibular nuclei.

Projections from the vestibular nuclei to the oculomotor system allow eye muscles to compensate for head movement by moving in such a way as to hold the image of the external world motionless on the retina. Sustained rotation results in a pattern of alternating slow and fast eye movements called nystagmus. The slow eye movement is equal and opposite to the head movement, whereas the fast eye movement represents a resetting movement in the opposite direction. Nystagmus in the absence of sustained head rotation is a sign of disease of the vestibular apparatus or its central connections. Vestibular signals habituate during sustained rotation and are relatively insensitive to very slow head movements.

Head movement evokes motion of the entire visual image on the retina as the moving eyes sweep across a stable visual field. This visual signal supplements the vestibular signal in the brain and compensates for the tendency of the vestibular signal to adapt during prolonged rotation. The optokinetic system provides the visual input to the central vestibular system. The motion of the retinal image induced by head movement enables the optokinetic system to induce eye movements and perceptions that are equivalent to those induced by actual head movement.

The vestibulo-ocular reflex is adaptable. If a process such as muscle weakness or visual distortion alters the relationship between the visual input and the motor output, the brain compensates for that change. This compensation requires activity in both the cerebellum and the vestibular nuclei.

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