Chapter 27: The Vestibular System

Introduction

MODERN VEHICULAR TRAVEL ON EARTH and through extraterrestrial space relies upon sophisticated guidance systems that integrate acceleration, velocity, and positional information through transducers, computational algorithms, and satellite triangulation. Yet the principles of inertial guidance are ancient: Vertebrates have used analogous systems for 500 million years and invertebrates for even longer. In these animals, the inertial guidance system, termed the vestibular system, serves to detect and interpret motion through space as well as orientation relative to gravity.

Through extensive research over many decades, it is apparent that most, if not all, organisms on Earth have evolved to sense one of the most prevalent "forces" in our universe, gravity. The mechanisms for the sensory transduction are as diverse as nature could devise. Gravity is most precisely referenced as gravito-inertial acceleration (GIA), a distinct form of linear acceleration directed toward the core of our planet. In truth, gravity varies systematically by as much as 0.5% between the equator and the poles; it increases over mineral-dense regions and decreases over mineral-light regions of the Earth's surface. Yet every single behavior that animals perform is referenced to the GIA, and all of our actions and cognitive directives depend upon knowledge of our motion and orientation relative to it. The first developments of what we refer to as a vestibular system were actually gravity sensors; as behavior became increasingly mobile, sensory organs evolved to process rotational accelerations as well.

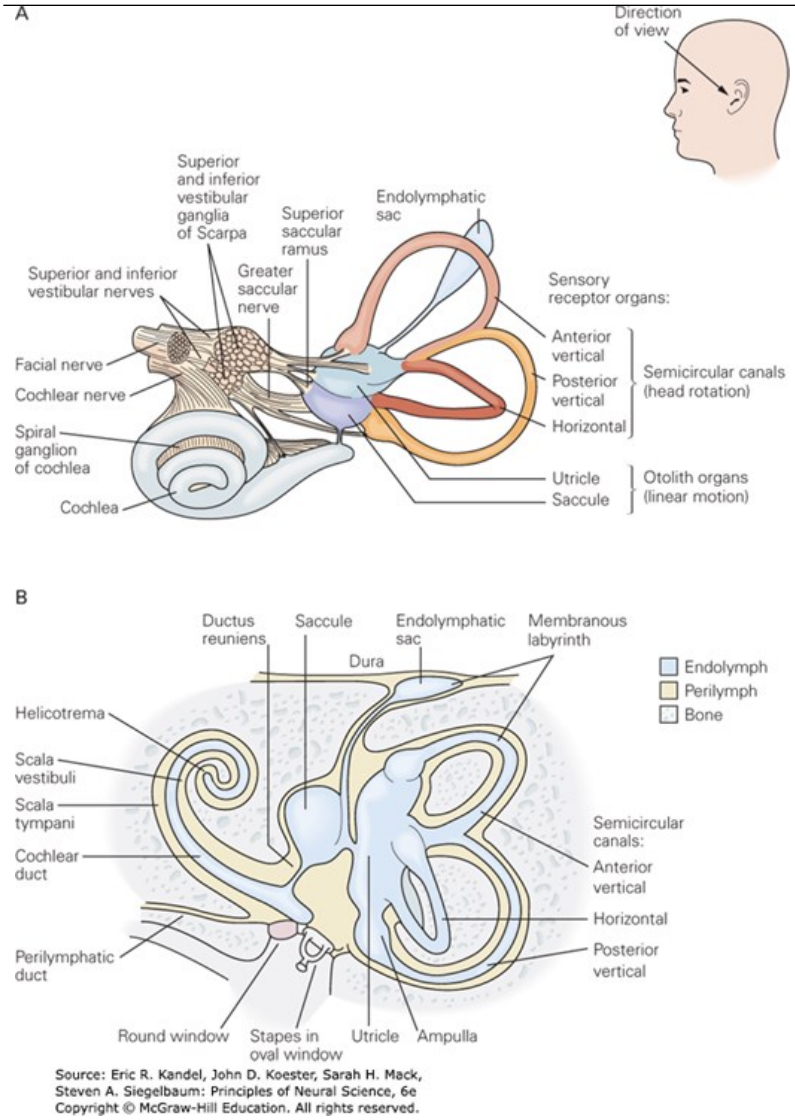
In this chapter we will concentrate on the vestibular system of vertebrates, which has remained highly conserved across many species. Vestibular signals originate in the labyrinths of the internal ear (Figure 27–1B). The *bony labyrinth* is a hollow structure within the petrous portion of the temporal bone. Within it lies the *membranous labyrinth,* which contains sensors for both the vestibular and auditory systems.

Figure 27–1

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 petrosal 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 from Iurato 1967.)



The vestibular receptors consist of two parts: two otolith organs, the utricle and saccule, which measure linear accelerations, and three semicircular canals, which measure angular accelerations. Rotational motion (angular acceleration) is experienced during head turns, whereas linear acceleration occurs during walking, falling, vehicular travel (ie, translations), or head tilts relative to gravity. These receptors send vestibular information to the brain, where it is integrated into an appropriate signal regarding direction and speed of motion, as well as the position of the head relative to the GIA. Many of the central vestibular neurons at the first junction with receptor afferent fibers also receive convergent signals from other systems such as proprioceptors, visual signals, and motor commands. Central processing of these multimodal signals occurs very rapidly to ensure adequate coordination of visual gaze and postural responses, autonomic responses, and awareness of spatial orientation.

The Vestibular Labyrinth in the Inner Ear Contains Five Receptor Organs

The membranous labyrinth is supported within the bony labyrinth by a filamentous network of connective tissue. The vestibular portion of the membranous labyrinth lies lateral and posterior to the cochlea. Vestibular receptors are contained in specialized enlarged regions of the membranous labyrinth, termed the ampullae for the semicircular canals and maculae for the otolith organs (Figure 27–1B). Both of the otolith organs lie in a central compartment of the membranous labyrinth, the vestibule, which is surrounded by the bony labyrinth of the same name.

The membranous labyrinth is filled with endolymph, a K^+-rich (150 mM) and Na^+-poor (16 mM) fluid whose composition is maintained by the action of ion pumps in specialized cells. Endolymph bathes the surface of the vestibular receptor 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^+ (150 mM), low-K^+ (7 mM) fluid similar in

composition to cerebrospinal fluid, with which it is in communication through the cochlear duct. Perilymph bathes the basal surface of the receptor epithelia and the vestibular nerve fibers. Two fluid-tight partitions in the bony labyrinth, the oval and round windows (Figure 27–1B), connect the perilymphatic space to the middle ear cavity. The oval window is connected to the tympanic membrane by the middle ear ossicles. These windows are important for sound transduction (Chapter 26). The endolymph and perilymph are kept separate by a junctional complex of support cells that surrounds the apex of each receptor cell. Disruption of the balance between these two fluids (by trauma or disease) can result in vestibular dysfunction, leading to dizziness, vertigo, and spatial disorientation.

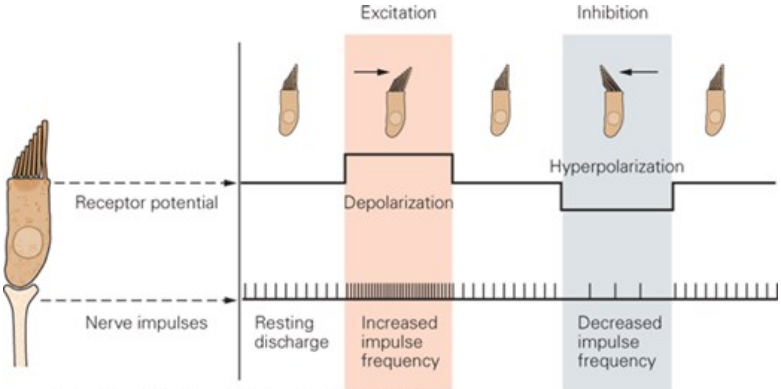
During development, the labyrinth progresses from a simple sac to a complex set of interconnected sensory organs, but retains the same fundamental topological organization. Each organ originates as an epithelium-lined pouch that buds from the otic cyst, and the endolymphatic spaces within the several 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 27–1B). In addition, the membranous labyrinth contains a small tube, the endolymphatic duct, which extends through a space in the sigmoid bone, the vestibular aqueduct, to end in a blind sac adjacent to the dura in the epidural space of the posterior cranial fossa. It is thought that the endolymphatic sac has both absorptive and excretive functions to maintain the ionic composition of the endolymphatic fluid.

Hair Cells Transduce Acceleration Stimuli Into Receptor Potentials

Each of the five receptor organs has a cluster of hair cells responsible for transducing head motion into vestibular signals. Hair cells are so named due to an array of nearly 100 staggered height stereocilia. The shortest stereocilia are at one end of the cell and the tallest at the other, ending with the only true cilium of the hair cell, termed the kinocilium. The kinocilium is typically the tallest of all stereocilia. Angular or linear acceleration of the head leads to a deflection of the stereocilia, which together compose the hair bundle (Figure 27–2).

Figure 27–2

Hair cells in the vestibular labyrinth transduce mechanical stimuli into neural signals. At the apex of each cell are the stereocilia, which increase in length toward the single kinocilium. The membrane potential of the receptor cell depends on the direction in which the stereocilia are 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.)



Specialized ion channels in the tips of the hair bundle stereocilia allow K^+ to enter or be blocked from the surrounding endolymph (Chapter 26). This action allows hair cells to act as mechanoreceptors, where deflection of the stereocilia produces a depolarizing or hyperpolarizing receptor potential depending on which direction the hair bundle moves (Figure 27–2). These depolarizations and hyperpolarizations of the receptor membrane lead to excitation and inhibition, respectively, in the firing rate of the innervating afferent (Figure 27–2). In each vestibular receptor organ, hair cells are arranged so that movement directional specificity is defined by excitation in some cells and inhibition in other cells.

Vestibular signals are carried from the hair cells to the brain stem by branches of the vestibulocochlear nerve (cranial nerve VIII), which enter the brain stem and terminate in the ipsilateral vestibular nuclei, cerebellum, and reticular formation. Cell bodies of the vestibular nerve are located in Scarpa's ganglia within the internal auditory canal (Figure 27–1A). 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, travels with nerve VIII. 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.

All vertebrate receptor hair cells receive efferent inputs from the brain stem. The function of the efferent innervation of vestibular receptors is still a subject of debate. Stimulation of the efferent fibers from the brain stem changes the sensitivity of the afferent axons from the hair cells. It increases the excitability of some afferents and hair cells while inhibiting others, and varies across species.

The Semicircular Canals Sense Head Rotation

An object undergoes angular acceleration when its rate of rotation about an axis changes. Therefore, the head 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 motion directions to the brain.

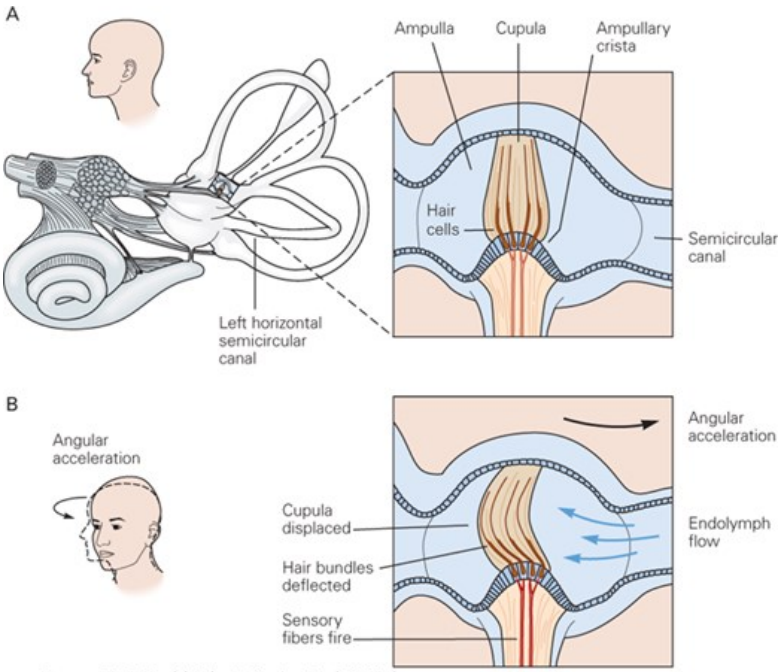
Each semicircular canal is a semicircular tube of membranous labyrinth extending from the vestibule. One end of each canal is open to the vestibule, whereas at the other end, the ampulla, the entire lumen of the canal is traversed by a fluid-tight gelatinous diaphragm, the cupula. The stereocilia and the kinocilium protrude into the gelatinous cupula, while the hair cells are located below in a receptor epithelium, the crista, along with the innervating afferent terminals (Figure 27–3).

Figure 27–3

The ampulla of a semicircular canal.

A. A thickened zone of epithelium, the ampullary crista, contains the hair cells. The stereocilia and the kinocilia 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 relative movement of endolymph when the head turns. As a result, the hair bundles are also displaced. Their movement is greatly exaggerated in the diagram.



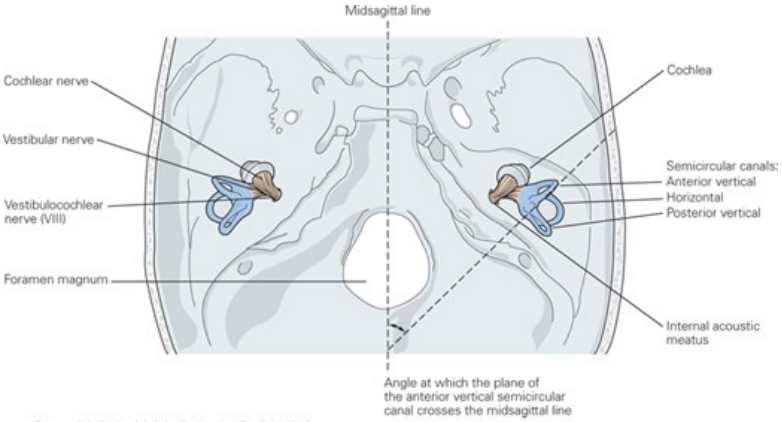
The vestibular organs detect accelerations of the head because the inertia of endolymph and cupula results in forces acting on the stereocilia. Consider the simplest situation, a rotation in the plane of a semicircular canal. When the head begins to rotate, the membranous and bony labyrinths move along with it. Because of its inertia, however, the endolymph lags behind the surrounding membranous labyrinth, thus pushing the cupula in a direction opposite that of the head (Figure 27–3B).

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 cup. If you continue rotating the cup at the same speed, the coffee (and the bubble) eventually catches up to the cup and rotates 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 vestibule, 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. Each semicircular canal is maximally sensitive to rotations in its plane. The horizontal canal is oriented approximately 30° elevated above the naso-occipital axis (roughly in the horizontal plane as a person walks and looks at the ground ahead) and thus is most sensitive to rotations in the horizontal plane. The stereocilia are arranged so that leftward rotational motion is excitatory for the left horizontal canal and inhibitory for the right horizontal canal. The anterior and posterior canals are oriented more vertically in the head, at an angle of approximately 45 degrees from the sagittal plane (Figure 27–4). Similar rotational motion downward in the plane of the anterior canals is excitatory for anterior canal hair cells, while upward head motion is excitatory for posterior canals.

Figure 27–4

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. The vertical semicircular canals lie nearly 45° from the midsagittal plane. Each of the semicircular canals on one side of the head lie in approximately orthogonal planes to each other.

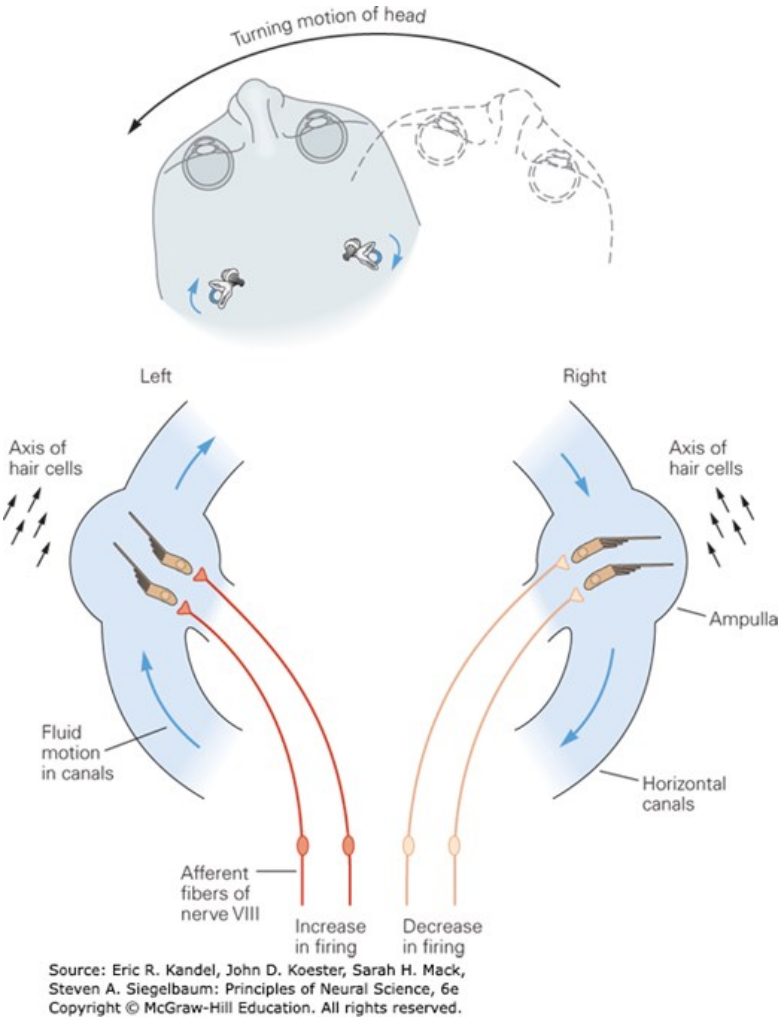


Because there is approximate mirror symmetry of the left and right labyrinths, the six canals effectively operate as three coplanar pairs. The two horizontal canals form one pair; each of the other pairs consists of one anterior canal on one side of the head and the contralateral posterior canal. Further, the three semicircular canals on each side of the head lie roughly orthogonal to each other (Figure 27–4). When the head moves toward the receptor hair cells (eg, leftward head turns for the left horizontal semicircular canal), the stereocilia are bent toward the tall kinocilium, thus exciting (depolarizing) the cell. Head motion in the opposite direction causes bending away from the kinocilum and toward the smallest stereocilia, thus closing the channels and inhibiting (hyperpolarizing) the cell.

The left and right ear semicircular canals have opposite polarity; thus, when you turn your head to the left, the receptors in the left horizontal semicircular canal will be excited (increased firing rate), whereas right horizontal canal receptors will be inhibited (decreased firing rate; Figure 27–5). The same relationship is true for the vertical semicircular canals. The canal planes are also roughly aligned to the pulling planes of specific 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 canal pair lie 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.

Figure 27–5

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.



The Otolith Organs Sense Linear Accelerations

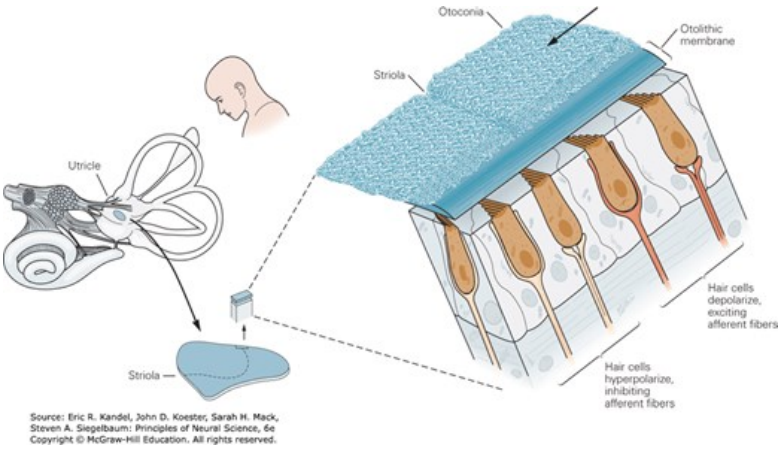
The vestibular system must compensate not only for head rotations but also for linear motion. The two otolith organs, the utricle and saccule, detect linear motion as well as the static orientation of the head relative to gravity, which is itself a linear acceleration. Each organ consists of a sac of 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*, which covers the entire macula (Figure 27–6). Embedded on the surface of this membrane are fine, dense particles of calcium carbonate called *otoconia* (Greek root translates to “ear dust”), which give the otolith (“ear stone”) organs their name. Otoconia are typically 0.5 to 30 µm long; thousands of these particles are attached to the otolithic membranes of the utricle and saccule.

Figure 27–6

The utricle detects 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. The directional polarity of each hair cell is organized relative to a reversal region running through the center of the utricle, termed the

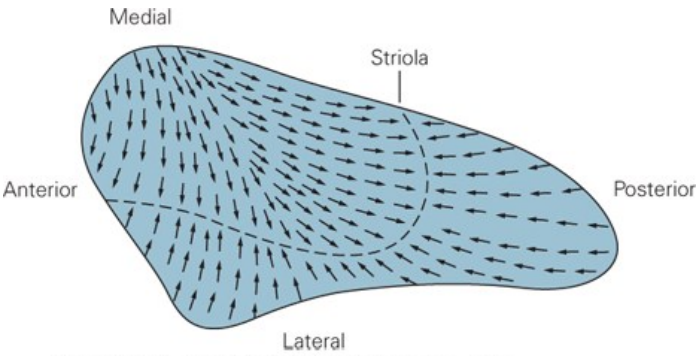
striola (see Figure 27–7). Thus, when the head is tilted, the gravitational force on the otoconia bends each hair bundle in a particular direction. When the head is tilted in the direction of a hair cell's axis of polarity, that cell depolarizes and excites the afferent fiber. When the head is tilted in the opposite direction, the same cell hyperpolarizes and inhibits the afferent fiber. (Adapted from Iurato 1967.)



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 raised above the naso-occipital axis by approximately 30°, similar to the horizontal semicircular canal. In normal resting head position, the utricle is deviated to bring the utricle approximately equal to an Earth horizontal plane. Any acceleration in the horizontal plane excites some hair cells in each utricle and inhibits others, according to their orientations (Figures 27–6 and 27–7).

Figure 27–7

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 containing the hair cells, 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.)



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

Central Vestibular Nuclei Integrate Vestibular, Visual, Proprioceptive, and Motor Signals

The vestibular nerve projects ipsilaterally from the vestibular ganglion mainly to four vestibular nuclei (medial, lateral, superior, and descending) in

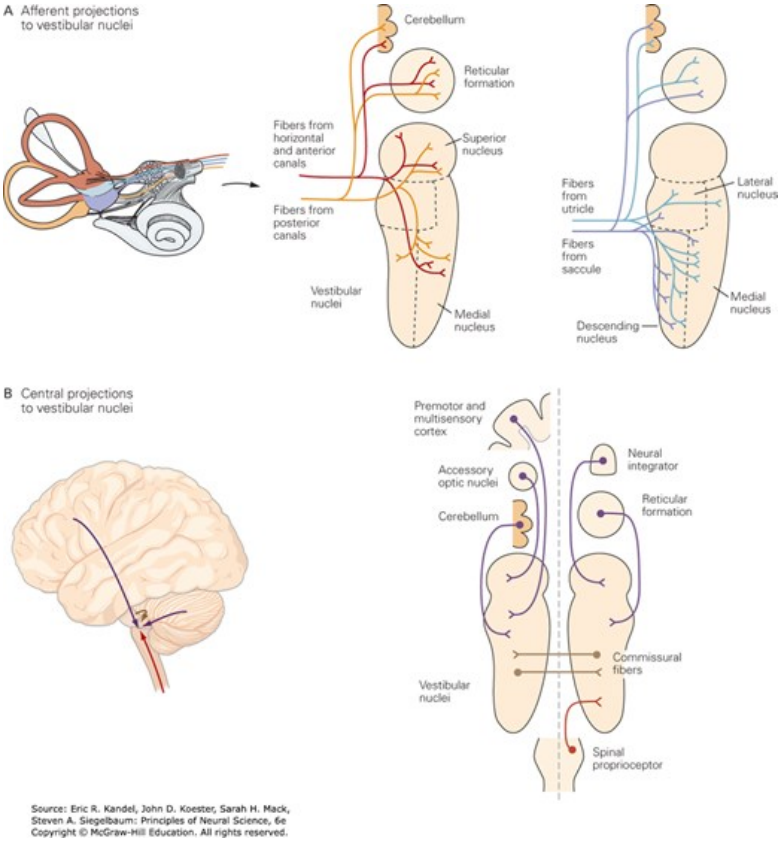
the dorsal part of the pons and medulla, in the floor of the fourth ventricle. Many vestibular nerve fibers also bifurcate, sending a direct projection to the fastigial nucleus, the nodulus and uvula, and the reticular formation (Figure 27–8A). These nuclei integrate signals from the vestibular organs with signals from the spinal cord, cerebellum, and visual system.

Figure 27–8

Afferent fiber and central projections to the vestibular nuclei.

A. Afferent fibers from vestibular receptors terminate in the brain stem and cerebellum. Fibers from semicircular canals project primarily to the medial portions of the superior and medial vestibular nuclei, the descending vestibular nucleus, the cerebellum (nodulus and uvula), and the reticular formation. Fibers from the otoliths primarily project to the lateral portions of all vestibular nuclei, the nodulus and uvula, and the reticular formation. (Adapted, with permission, from Gacek and Lyon 1974.)

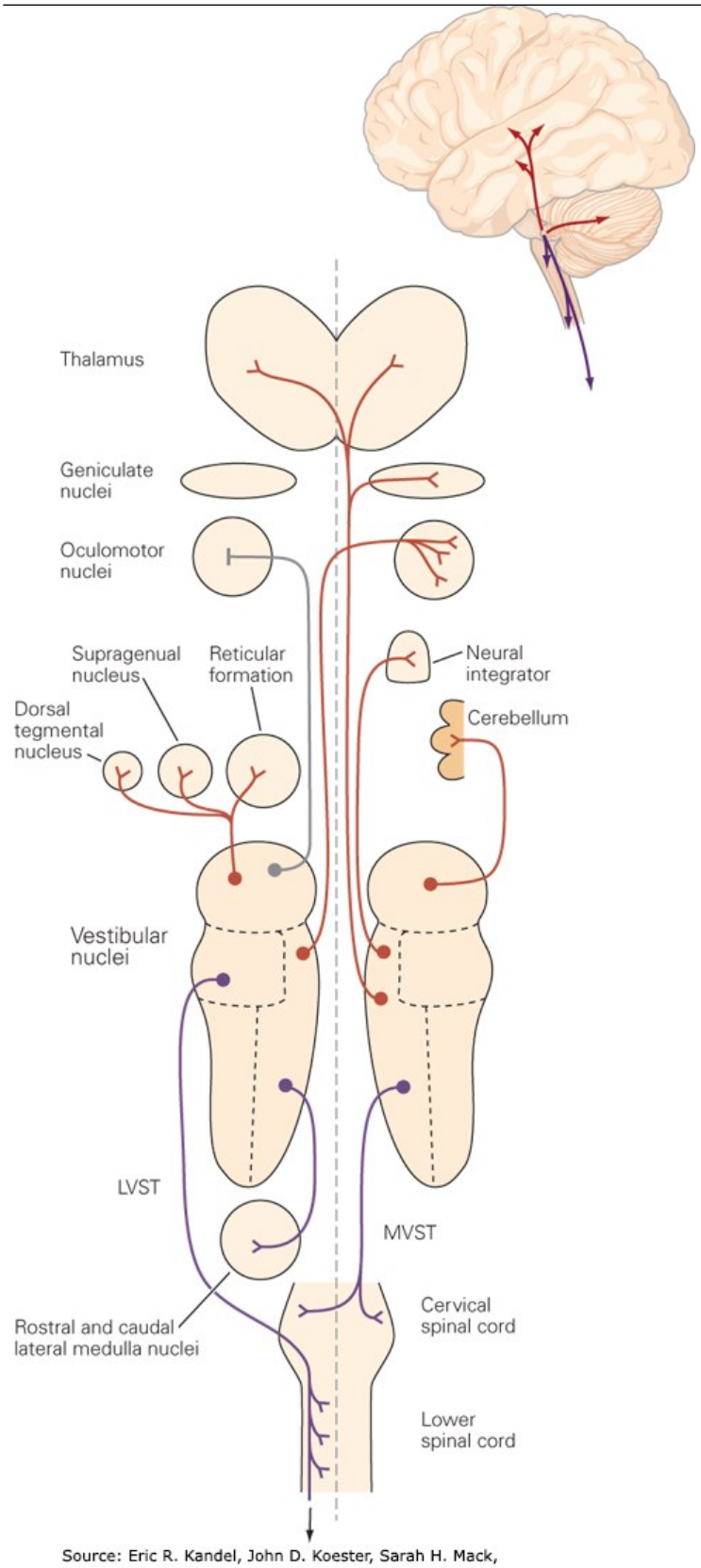
B. Central projections to the vestibular nuclei arise from a number of cortical, brain stem, and spinal cord regions. These include the premotor and multisensory cortices, accessory optic nuclei, cerebellum, neural integrator nuclei, reticular formation, spinal cord, and commissural fibers from the contralateral vestibular nuclei.



The vestibular nuclei project, in turn, to many central targets, including the oculomotor nuclei, reticular and spinal centers concerned with gaze and postural movement, and the thalamus (Figure 27–9). Many vestibular nuclei neurons have reciprocal connections with the cerebellum, primarily in the floculo-nodular lobe, that form important regulatory mechanisms for eye movements, head movements, and posture (Figures 27–8 and 27–9). The vestibular nuclei receive inputs from the premotor cortex, the accessory optic system (nucleus of the optic tract), the neural integrator nuclei (nucleus prepositus hypoglossi and interstitial nucleus of Cajal), and the reticular formation (Figure 27–8). Further projections from the vestibular nuclei reach the rostral and caudal lateral medulla nuclei that are involved in regulation of blood pressure, heart rate, respiration, and bone remodeling, as well as the parabrachial nucleus for homeostasis modulation. Finally, there are projections from the vestibular nuclei to the medial geniculate (auditory) nuclei, as well as the supragenual nucleus and dorsal tegmental nucleus, which contribute to spatial orientation (Figure 27–9).

Figure 27–9

(Left) Output projections from the vestibular nuclei. The vestibular nuclei project to a number of brain regions below the cortical level. Two separate descending pathways project through the lateral and medial vestibulospinal tracts (**LVST, MVST**) to terminate in the spinal cord. The vestibular nuclei also project to the reticular formation and the lateral medullary nuclei in the brain stem. Ascending projections to the supragenual nucleus, the dorsal tegmental nucleus, the oculomotor nuclei (abducens, oculomotor, and trochlear), and the neural integrator nuclei are very prominent (**red line**, excitatory; **gray line**, inhibitory), as are projections to the cerebellum (nuclei, nodulus, and uvula). Other prominent vestibular projections terminate in the geniculate nuclei and the thalamus (ventral lateral, posterior, and intralaminar thalamic regions).



Source: Eric R. Kandel, John D. Koester, Sarah H. Mack, Steven A. Siegelbaum: Principles of Neural Science, 6e

The superior and medial vestibular nuclei receive fibers predominantly from the semicircular canals in the medial regions and some otolith input in the lateral regions (Figure 27–8). They send fibers predominantly to the cerebellum, reticular formation, thalamus, oculomotor centers, and spinal

cord (Figure 27–9). Oculomotor center outputs include the three oculomotor nuclei (abducens, oculomotor, trochlear), as well as the neural integrators for converting head velocity into head position signals in the nucleus hypoglossi (horizontal eye movements) and interstitial nucleus of Cajal (vertical eye movements). These nuclei are described in some detail later.

Another major output pathway concerned with gaze control arises from the medial vestibular nucleus (as well as lesser projections from the descending and lateral vestibular nuclei) and projects bilaterally to the cervical spinal cord through the medial vestibulospinal tract (Figure 27–9; see Chapter 35). There are two categories of medial vestibulospinal fibers. Vestibulospinal neurons project only to the spinal cord to control neck musculature. Vestibulo-ocular neurons project to both the spinal cord and the oculomotor nuclei and are involved in coordinated eye and head movements to maintain gaze stability.

The lateral vestibular nucleus (Deiters' nucleus) receives fibers from the semicircular canals medially and the otolith organs laterally. There is a major output to all levels of the ipsilateral spinal cord through the lateral vestibulospinal tract that is concerned principally with postural reflexes through modulation of limb and axial musculature (Figure 27–9). Lateral vestibular nuclei neurons also project heavily to the reticular formation. The descending vestibular nucleus receives predominantly otolithic input, but also receives semicircular canal fibers medially, and projects to the cerebellum, reticular formation, and spinal cord (medial vestibulospinal tract). The primary neurotransmitters for excitatory vestibular nuclear projections include glutamate, whereas the inhibitory projections are either glycine or γ-aminobutyric acid (GABA). Vestibular projections to the spinal systems are discussed in more detail in Chapter 36.

The Vestibular Commissural System Communicates Bilateral Information

Many of these vestibular nuclei neurons receive convergent motion information from the opposite ear through an inhibitory commissural pathway that uses GABA as a neurotransmitter (Figure 27–8B). The commissural pathway is highly organized according to the type of receptor from which information is received. For example, cells receiving signals from the ipsilateral horizontal excitatory canal will also receive signals from the contralateral horizontal canal through an inhibitory interneuron. Due to the directional selectivity of the receptors in each ear, the contralateral horizontal canal input will always be decreased during an ipsilateral head turn, in effect "disinhibiting" the inhibitory input from the contralateral side.

The effect of the commissural system is to increase the response of the vestibular nuclei neuron and decrease noise from the incoming afferent signal, giving rise to a "push-pull" vestibular function. From an engineering point of view, the "push-pull" set point in the nuclei neurons constantly updates canal signals from the opposing ear to act as a comparator junction and can explain the relatively high spontaneous firing rate of canal afferents at nearly 100 spikes/s. For example, during a leftward head turn, left brain stem nuclei neurons receive high firing rate signals from the left horizontal canal and low firing rate signals from the right horizontal canal. The comparison of activity is interpreted as a left head turn (Figure 27–5). Similar comparisons between signals also occur for inputs from the anterior semicircular canal on one side and the posterior semicircular canal on the opposite ear side. Thus, for rotational motion in any head plane, the comparator is able to determine the direction of movement with great specificity.

Any disruption of the normal balance between left and right ear canal inputs (eg, from trauma or disease in the receptor organs or nerve) will be interpreted by the brain as a head rotation, even though the head is stationary. These effects often lead to illusions of spinning or rotating that can be quite upsetting and may produce nausea or vomiting. However, over time, the commissural fibers provide for vestibular compensation, a process by which the loss of unilateral vestibular receptor function is partially restored centrally and behavioral responses such as the vestibulo-ocular reflex mostly recover.

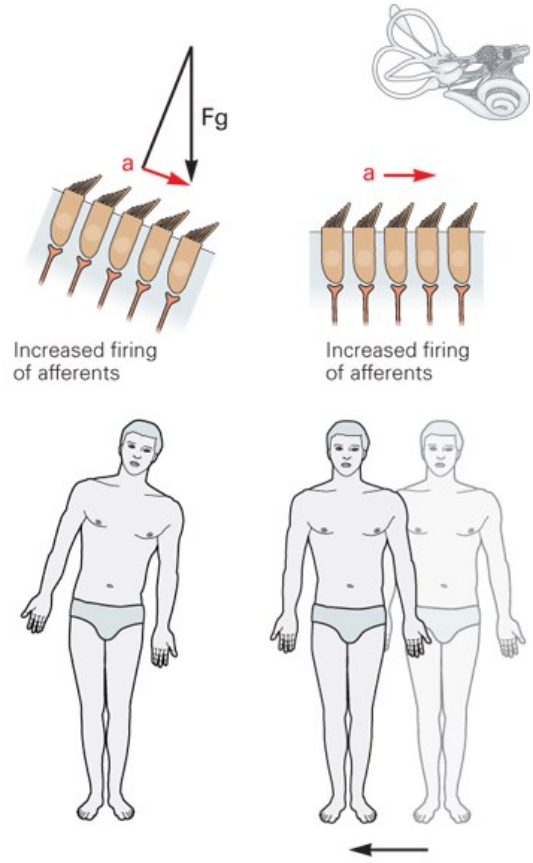
Combined Semicircular Canal and Otolith Signals Improve Inertial Sensing and Decrease Ambiguity of Translation Versus Tilt

In some instances, the vestibular input from a single receptor may be ambiguous. For example, Einstein (1908) showed that linear accelerations are equivalent whether they arise from translational motion or tilts of the head relative to gravity. The otolith receptors cannot discriminate between the two: So how is it that we can tell the difference between translating rightward and tilting leftward, where the linear acceleration signaled by the otolith afferents is the same (Figure 27–10)?

Figure 27–10

Vestibular inputs signaling 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*).



It is now well established that convergent vestibular nuclei and cerebellar neurons use combined signals from both the semicircular canals and the otolith receptors and some simple computations to discriminate between tilt and translation. As a result, some central vestibular and cerebellar cells encode head tilt, whereas other cells encode translational motion, which, as we will see, is extremely important for the control of head and eye movements.

Vestibular Signals Are a Critical Component of Head Movement Control

An important discovery is the differing responses in some vestibular nuclei neurons to actively versus passively generated head movements. Specifically, in contrast to vestibular afferents, some neurons in the vestibular nuclei and cerebellum well known for responding to vestibular stimuli during passive movement lose or reduce their sensitivity during self-generated movement. The preferential response to passive motion, or to the passive components of combined active and passive motion, has been interpreted as sensory prediction error signals: The brain predicts how self-generated motion activates the vestibular organs and subtracts these predictions from afferent signals. Such error signals are important for the on-line control of head movement, as well as head movement estimation.

Computationally, these properties have been interpreted quantitatively using concepts common to all sensorimotor systems; that is, active and passive motion signals are processed by internal models of the motion sensor (ie, the canals, otolith organs, and neck proprioceptors). The brain uses an internal representation of the laws of physics and sensory dynamics (which can be elegantly modeled as forward internal models of the sensors) to process vestibular signals. Without such error signals, accurate self-motion estimation would be severely compromised. These computational insights suggest that, unlike early interpretations, vestibular signals remain critically important when coupled to self-motion estimation and head movement control during actively generated head movements.

Vestibulo-Ocular Reflexes Stabilize the Eyes When the Head Moves

In order to see clearly and maintain focus on visual objects during head motion, the eyes maintain foveal fixation through a series of vestibulo-ocular reflexes (VORs). If you shake your head back and forth while reading, you can still discern words because of the VORs. If instead you move the book at a similar speed while holding your head steady, you can no longer read the words.

In the latter instance, vision provides the brain with the only corrective feedback for stabilizing of the image on the retina, and visual processing in vertebrates is much slower (around 100 ms latency) and less effective than vestibular processing (around 10 ms) 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 two components of VORs. The *rotational VOR* compensates for head rotation and receives its input predominantly from the semicircular canals. The *translational VOR* compensates for linear head movement. These two VOR responses arise from connections from vestibular nuclei neurons to the abducens, oculomotor, and trochlear nuclei (Figure 27–9).

The Rotational Vestibulo-Ocular Reflex Compensates for Head Rotation

When the semicircular canals sense head rotation in one direction, the eyes rotate in the opposite direction at equal velocity in the orbits (Figure 27–11). 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. During fast head movements, the VOR must act quickly to maintain stable gaze. A trisynaptic pathway, the three-neuron arc, connects each semicircular canal to the appropriate eye muscle (Figure 27–11).

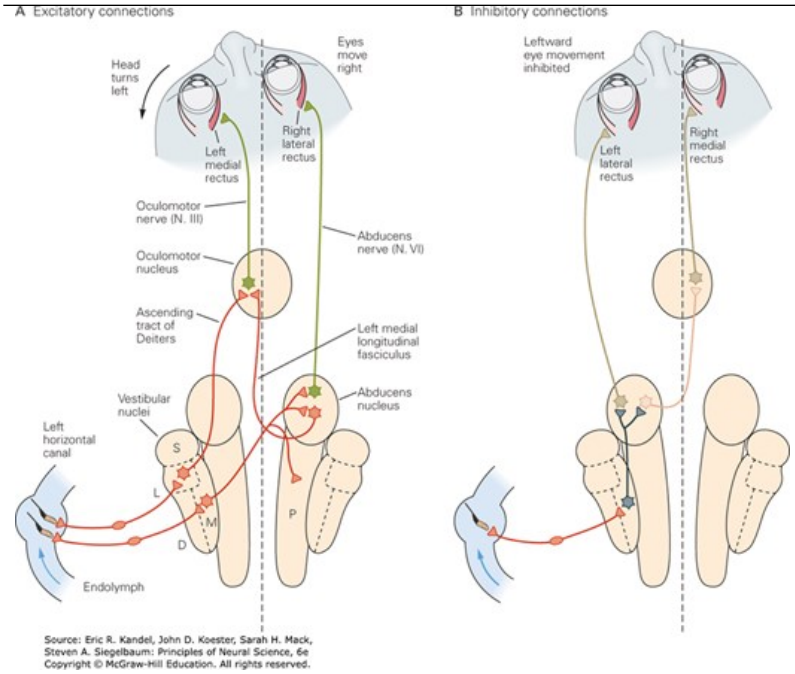
Figure 27–11

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 from Sugiuchi et al. 2005.)



The rotational VOR represents a phylogenetically old reflex. Many invertebrates and all vertebrate species, from amphibians, reptiles, fish, and birds to nonhuman primates, have the ability to reflexively rotate their eyes opposite to the direction of head rotation, thus keeping the visual world stable on the retina. Primary afferents from the horizontal semicircular canals send excitatory signals through the vestibular nuclei and the medial longitudinal fasciculus to the contralateral abducens nucleus (Figure 27–11). Abducens motor neurons send impulses via cranial nerve VI to excite the ipsilateral lateral rectus muscle. At the same time, abducens interneurons send excitatory signals to motor neurons in the contralateral oculomotor nucleus, which innervates the medial rectus muscle (see Chapter 35 for details on other projections).

The three-synapse pathway illustrated in Figure 27–11 is not sufficient to elicit appropriate compensatory eye movements. This is because the afferent signal from the semicircular canals is proportional to head velocity, while the compensatory eye movement requires eye position changes. To convert velocity to position requires temporal integration (simple calculus) that occurs through neural networks in the brain stem nuclei for most head motion speeds. However, at high rotation frequencies, the viscoelastic properties of the eyeball, eye muscles, and surrounding tissues provide an additional integration step. Thus, the rotational VOR is thought to consist of two parallel processes.

The first process consists of the direct neural pathway known as the three-neuron arc (Figure 27–11). The second neural integrator process consists of additional parallel pathways that ensure that the correct proportion of velocity and position commands are delivered to the oculomotor nuclei to move the eye appropriately (Figure 27–9 and see Chapter 35). Without this second indirect integrator pathway, the response to a head rotation would initially bring the eye to the correct position, but the eye would drift away from that position since the oculomotor neurons would lack the tonic input to compensate for the elastic restoring forces of the eyeball (Chapter 35). This is exactly what happens after lesions of brainstem and cerebellar structures that are thought to participate in this neural integration (eg, the prepositus hypoglossi and the interstitial nucleus of Cajal; Figure 27–9). It is generally thought that the integrator pathway is shared by all conjugate eye movement systems (saccades, smooth pursuit, and the VOR), although the direct pathway is at least partly segregated for different types of eye movements (ie, VOR, smooth pursuit, saccades).

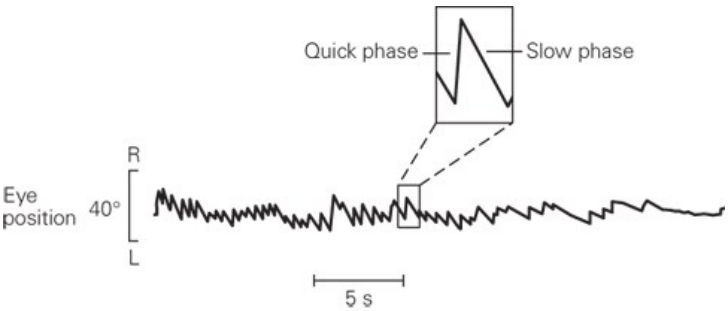
With continued head rotation, the eyes eventually reach the limit of their orbital range and stop moving. To prevent this, a rapid saccade-like movement called a quick phase displaces the eyes to a new point of fixation in the direction of head rotation.

If rotation is prolonged, the eyes execute alternating slow and quick phases called *nystagmus* (Figure 27–12). Although the slow phase is the primary response of the rotational VOR, the direction of nystagmus is defined in clinical practice by the direction of its quick phase. Since prolonged rightward rotation excites the right horizontal canal and inhibits the left horizontal canal, leftward slow phases and a *right-beating nystagmus* result.

Figure 27–12

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 2015.)



If the angular velocity of the head remains constant, the inertia of the endolymph is eventually overcome, as in the earlier coffee cup example. The cupula relaxes and vestibular nerve discharge returns to its 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 in darkness. Further, the same rotation in the presence of a visual surround activates the optokinetic reflex (Chapter 35) and elicits a steady-state nystagmus pattern that is sustained indefinitely. The interactions between canal and optokinetic signals during rotation occurs through the velocity storage network.

If head rotation stops abruptly, the endolymph continues to be displaced 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 suppress postrotatory nystagmus since there is no visual motion stimulus.

The Translational Vestibulo-Ocular Reflex Compensates for Linear Motion and Head Tilts

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 needed eye movement. During linear movements that do not involve head rotation, an appropriate translational VOR is elicited, driven by input from the otolith organs. Neurons in the vestibular nuclei, including some different from those providing the main drive to the rotational VOR, carry this signal to the extraocular motor neuron pools.

Side-to-side head movements result in a horizontal eye movement in a direction opposite to the head movement. Vertical displacements of the body, such as during walking or running, elicit oppositely directed vertical eye movements to stabilize gaze. However, in contrast to the rotational VOR where a head rotation is compensated by an equal but opposite eye rotation, horizontal displacement must be compensated by an eye rotation that depends on the viewed object distance, a nontrivial computation. For example, during a lateral head displacement, nearby objects move on the retina more rapidly than distant ones. So, in order to stabilize a nearby object on the retina, the eyes need to rotate by a larger amount than is needed for a distant object. Thus, the horizontal compensatory eye movements that are elicited during lateral motion scale with target distance; the closer the target, the larger is the compensatory eye movement. Similarly, as in the rotational VOR, compensatory responses to translation occur at relatively short latency (10–12 ms).

Fore-aft translations produce converging and diverging eye movements that bring the eyes together or move them apart. The amount of convergence or divergence is also dependent upon visual target distance, such that close visual objects produce large eye movements and distant visual objects produce little eye movements. Further, the amount of relative left and right eye movement is dependent upon visual object eccentricity relative to

straight ahead. Unlike the rotational VOR that is a full-field image stabilization reflex, the goal of the translational VOR is to selectively stabilize visual objects on the fovea. In general, the two eyes move disjunctively, consisting of either a pure vergence movement or a combination of vergence and conjugate eye movements. In practice, although the direction of the evoked eye movement is typically consistent with geometrical predictions, the primate/human translational VOR typically undercompensates for near-target viewing, with gains of only about 0.5.

The translational VOR differs from the rotational VOR in the ability to generate compensatory eye movements during translation that optimize visual acuity on the central retina. These abilities appear to be specific to frontal-eyed animals, such as primates. Many lateral-eyed species, like the rabbit, do not generate eye movements that compensate for the visual consequences of translation during self-motion.

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 to reduce the tilt of the retinal image. This ocular counter-rolling reflex—the ability to use a gravity-sensing mechanism to maintain gaze relative to the horizon—is of paramount importance for lateral-eyed, afoveate species that typically lack a well-developed saccadic system. But such functional utility for these tilt responses has lost its advantage in the primate oculomotor system, where static ocular counter-rolling and counter-pitching in humans have a gain of less than 0.1.

Vestibulo-Ocular Reflexes Are Supplemented by Optokinetic Responses

The VORs compensate for head 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 low-amplitude linear accelerations.

Thus, vestibular responses during prolonged motion in the light are supplemented by visual stabilization reflexes that maintain nystagmus when vestibular input ceases: optokinetic nystagmus, a full-field stabilization system, and ocular following, a foveal stabilization system. Although the two classes of reflexes are distinct, their pathways overlap.

The Cerebellum Adjusts the Vestibulo-Ocular Reflex

As we have seen, the VOR 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 VOR, however, would prevent your eyes from turning with your head. To prevent this sort of biologically inappropriate response, the VOR is under the control of the cerebellum and cortex, which suppress the reflex during volitional head movements.

In addition, the VOR 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). Indeed, the VOR is a highly modifiable reflex. The brain continuously monitors its performance by evaluating the clarity of vision during head movements. When head turns are consistently associated with image motion across the retina, the VOR undergoes gain changes in the direction appropriate to improve the compensatory ability of the reflex. For example, when viewing the world through spectacles that magnify or miniaturize the visual scene, the rotational VOR gain (in darkness) increases or decreases accordingly. The reflex behavior can adapt over several minutes, hours, and days. 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, rotational retinal image motion is zero, and there is no error.

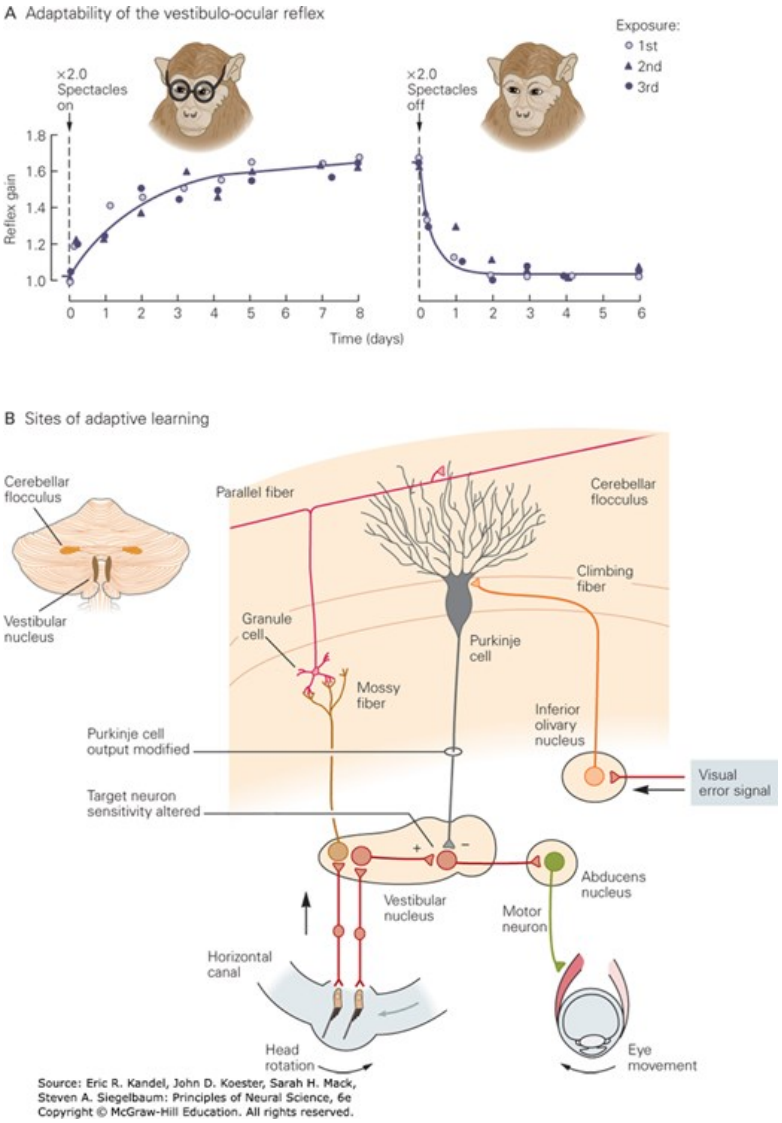
Anyone who wears eyeglasses depends on this plasticity of the VOR. Because lenses for nearsightedness shrink the visual image, a smaller eye rotation is needed to compensate for a given head rotation, and the gain of the VOR must be reduced. Conversely, glasses for farsightedness magnify the image, so the VOR gain must increase during their use. More complicated is the instance of bifocal or progressive spectacles, in which the reflex must use different gains for the different magnifications. In the laboratory, the 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 reflex gain gradually increases (Figure 27–13A).

Figure 27–13

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.



This process requires changes in synaptic transmission in both the cerebellum and the brain stem. If the flocculus and paraflocculus of the cerebellum are lesioned, the gain of the VOR can no longer be modulated. Mossy fibers carry vestibular, visual, and motor signals from the pontine and vestibular nuclei to the cerebellar cortex; the granule cells, with their parallel fiber axons, relay these signals to the Purkinje cells (Figure 27–13B). The synaptic efficacy of parallel fiber input to a Purkinje cell could be modified by the concurrent action of climbing fiber input. Indeed, the climbing fiber input to the cerebellum carries a retinal error signal, thought to serve as a "teaching" signal enabling the cerebellum to correct the error in the VOR. This adaptation requires long-term plasticity of multiple mechanisms through multiple sites (Chapter 37).

In addition to the Purkinje cell, plasticity is also found in the vestibular nuclei, in a particular class of neurons known as flocculus target neurons, which receive GABAergic inhibitory input from Purkinje cells in the flocculus as well as direct inputs from vestibular sensory fibers. During adaptation of the

VOR, 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, who are often characterized by a VOR response of abnormal amplitude or direction.

The Thalamus and Cortex Use Vestibular Signals for Spatial Memory and Cognitive and Perceptual Functions

For decades, vestibular function has been studied primarily in relation to reflexes, both vestibulo-ocular and vestibulospinal. Yet, in the past decade, it has become increasingly clear that the function of the vestibular system is as important for cognitive processes as for reflexes. The difficulty in understanding the vestibular system's role in spatial cognition stems from the fact that these functions are inherently multisensory, arising through convergence of vestibular, visual, somatosensory, and motor cues, following principles that remain poorly understood. Some of these perceptual functions of the vestibular system include tilt perception, visual-vertical perception, and visuospatial constancy.

Tilt perception. Vestibular information is critical for spatial orientation—the perception of how our head and body are positioned relative to the outside world. Nearly all species orient themselves using gravity, which provides a global, external reference. Thus, spatial awareness is governed by our orientation relative to gravity, collectively typically referred to as tilt.

Visual-vertical perception. We commonly experience the visual scene as perceptually oriented relative to earth-vertical orientation, regardless of our spatial orientation in the world. This ability has been studied psychophysically in humans and monkeys using tasks in which a subject is turned ear-down in the dark and asked to orient a dimly lit bar vertically in space (to align it with gravity). The results suggest that the neural representation of the visual scene is modified by static vestibular and proprioceptive signals that indicate the orientation of the head and body.

Visuospatial constancy. Vestibular signals are also important for the perception of a stable visual world despite constantly changing retinal images caused by movement of the eyes, head, and body. The projection of the scene onto the retina continuously changes because of these movements. Despite the changing retinal image, the percept of the scene as a whole remains stable; this stability is critical not only for vison but also for sensorimotor transformations (eg, to update the motor goal of an eye or arm movement).

Vestibular Information Is Present in the Thalamus

Vestibular projections to the thalamus are complicated and overall less clear, partly because of the strong multisensory nature of the responses in these cells and the difficulty in comparing thalamic regions and nomenclature across studies and species. Some neurons in all vestibular nuclei and likely the fastigial cerebellar nuclei project bilaterally to the thalamus, but most fibers terminate in the contralateral thalamic nuclei (Figure 27–9).

Several major thalamic regions receive vestibular projections, including the ventral posterolateral and ventral lateral thalamic nuclei and, to a lesser extent, the ventral posteroinferior nuclei, the posterior group, and the anterior pulvinar. These nuclei are traditionally thought to also receive somatosensory input and project to the primary and secondary somatosensory cortices, as well as the posterior parietal cortex (areas 5 and 7) and the insula of the temporal cortex.

Vestibular Information Is Widespread in the Cortex

A number of cortical areas receiving short-latency vestibular signals either alone or more commonly in concert with proprioceptive, tactile, oculomotor, visual, and auditory signals have been identified (Figure 27–14). Although vestibular signals are widely distributed to a number of cortical regions, all such regions are multimodal and none seems to represent a purely vestibular cortex, similar to other modalities such as vision, proprioception, and audition.

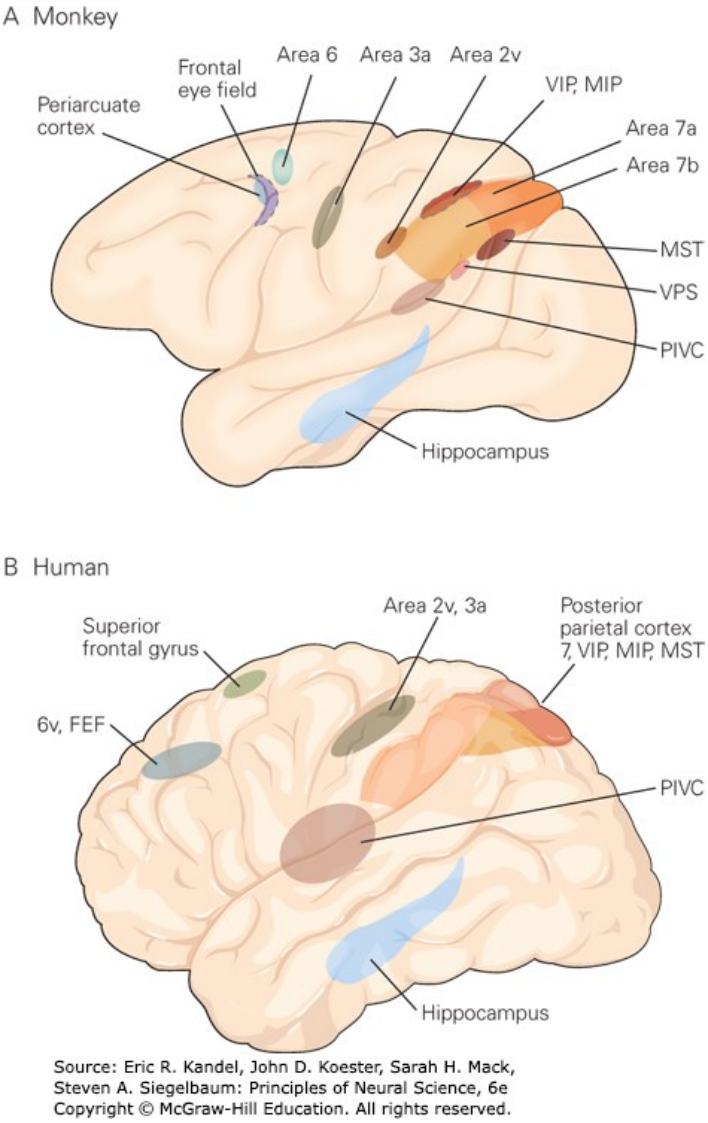
Figure 27–14

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. Areas in monkey cortex include periarcuate cortex, area 6, frontal eye fields, areas 3a and 2v, ventral intraparietal area (**VIP**), medial intraparietal area (**MIP**), area 7, visual posterior sylvian area (**VPS**), medial superior temporal area (**MST**), parieto-insular vestibular cortex (**PIVC**), and the hippocampal formation.

B. In the human cortex, areas recording vestibular activity include 6v, frontal eye fields (**FEF**), superior frontal gyrus, 2v, 3a, posterior parietal cortex,

PIVC, and the hippocampal formation.



Source: Eric R. Kandel, John D. Koester, Sarah H. Mack, Steven A. Siegelbaum: Principles of Neural Science, 6e

Vestibular modulation has been established in the lateral sulcus (parietoinsular vestibular cortex), somatosensory cortex (areas 3a and 2v), oculomotor cortex (frontal and supplementary eye fields), extrastriate visual motion cortex (dorsal medial superior temporal area), and parietal cortex (ventral intraparietal area and area 7a). In the primary somatosensory cortex, area 2v lies at the base of the intraparietal sulcus just posterior to the areas of the postcentral gyrus representing the hand and mouth. Electrical stimulation of area 2v in humans produces sensations of whole-body motion. Area 3a lies at the base of the central sulcus, adjacent to the motor cortex. Many cells in the parietoinsular vestibular cortex are multisensory, responding to body motion, somatosensory, proprioceptive, and visual motion stimuli. Patients with lesions in this region report episodes of vertigo, unsteadiness, and a loss of perception for visual vertical. Neurons in the medial intraparietal and medial superior temporal areas respond to both visual (optic flow) and vestibular signals. These cells utilize multisensory cue integration (Bayesian) frameworks to assist in the cognitive perception of motion through space.

Imaging studies reveal an even larger portion of cerebral cortex involved in processing vestibular information, including the temporoparietal cortex and the insula, the superior parietal lobe, the pre- and postcentral gyri, anterior cingulate and posterior middle temporal gyri, premotor and frontal cortices, inferior parietal lobule, putamen, and hippocampal regions. Using electrical stimulation of the vestibular nerve in patients activates the prefrontal lobe and anterior portion of the supplementary motor area at relatively short latencies. However, imaging and, to a lesser extent, single-cell recording studies may overstate the range of vestibular representations. In particular, vestibular stimuli often co-activate the somatosensory and proprioceptive systems, as well as evoke postural and oculomotor responses, which might in turn result in increased cortical activations.

Vestibular Signals Are Essential for Spatial Orientation and Spatial Navigation

Our ability to move about depends on a stable directional orientation. Certain cells in the thalamus, hippocampal region, entorhinal cortex, and subiculum are involved in navigation tasks. Damage to these areas impairs a variety of spatial and directional abilities. At least six cell types contributing to spatial orientation have been identified, including place cells, grid cells, head direction cells, border cells, speed cells, and conjunctive cells. In the hippocampus, place cells discharge relative to the animal's location in the environment (Chapter 54). Head direction cells in the dorsal thalamus, parahippocampal regions, and several regions of the cortex indicate the animal's heading direction like a compass. Grid cells in the entorhinal cortex respond to multiple spatial locations in a unique triangular grid pattern. Border cells in the entorhinal cortex signal environmental boundaries, speed cells discharge in proportion to the animal's running speed, and conjunctive cells exhibit a combination of several of these properties.

These regions are intimately connected and appear to work together in a "navigation network" to provide for spatial orientation, spatial memory, and our ability to move through our surroundings. Think of walking through your house, driving to the store, or knowing which direction to go in a new city. Lesions of central vestibular networks disrupt head direction, place, and grid responses. Patients with disease or trauma to the vestibular system, hippocampus, and anterior thalamus regions often exhibit severe deficits in their ability to orient in familiar environments or even find their way home.

All of these cells depend on a functioning vestibular system to maintain their spatial orientation properties. The pathway by which vestibular signals reach the navigation network and the computational principles determining how vestibular cues influence these spatially tuned cells is not well understood. We know that there are at least three different influences: Semicircular canal signals contribute to the estimate of head direction; gravity signals influence the three-dimensional properties of head direction cells; and translation signals influence the estimate of linear speed, which controls both grid cell properties and the magnitude and frequency of theta oscillations in the hippocampal network. What is clear is that there is no evidence linking vestibular nuclei response properties directly to head direction or other spatially tuned cell types, and no direct projections from the vestibular nuclei to the brain areas thought to house these spatially tuned neurons have been identified. Furthermore, vestibular nuclei responses are inappropriate for driving these spatially tuned cells, as these signals need to encompass the total head movement, rather than individual components during active or passive head movement.

It has long been recognized that proprioceptive and motor efference cues should participate, together with vestibular signals, to track head direction over time. It has been proposed that internally generated information from vestibular, proprioceptive, and motor efference cues can be utilized to keep track of changes in directional heading. More recent insights have started to shed light on how each of these cues contributes to the final self-motion estimate that can be precisely predicted and quantitatively estimated based on a Bayesian framework. Although as yet difficult to define, quantitative internal models govern the relationship of vestibular and other multisensory self-motion cues for computing the spatial properties of navigation circuit cells.

Clinical Syndromes Elucidate Normal Vestibular Function

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 in the canals oriented away from the motion direction. 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.

Caloric Irrigation as a Vestibular Diagnostic Tool

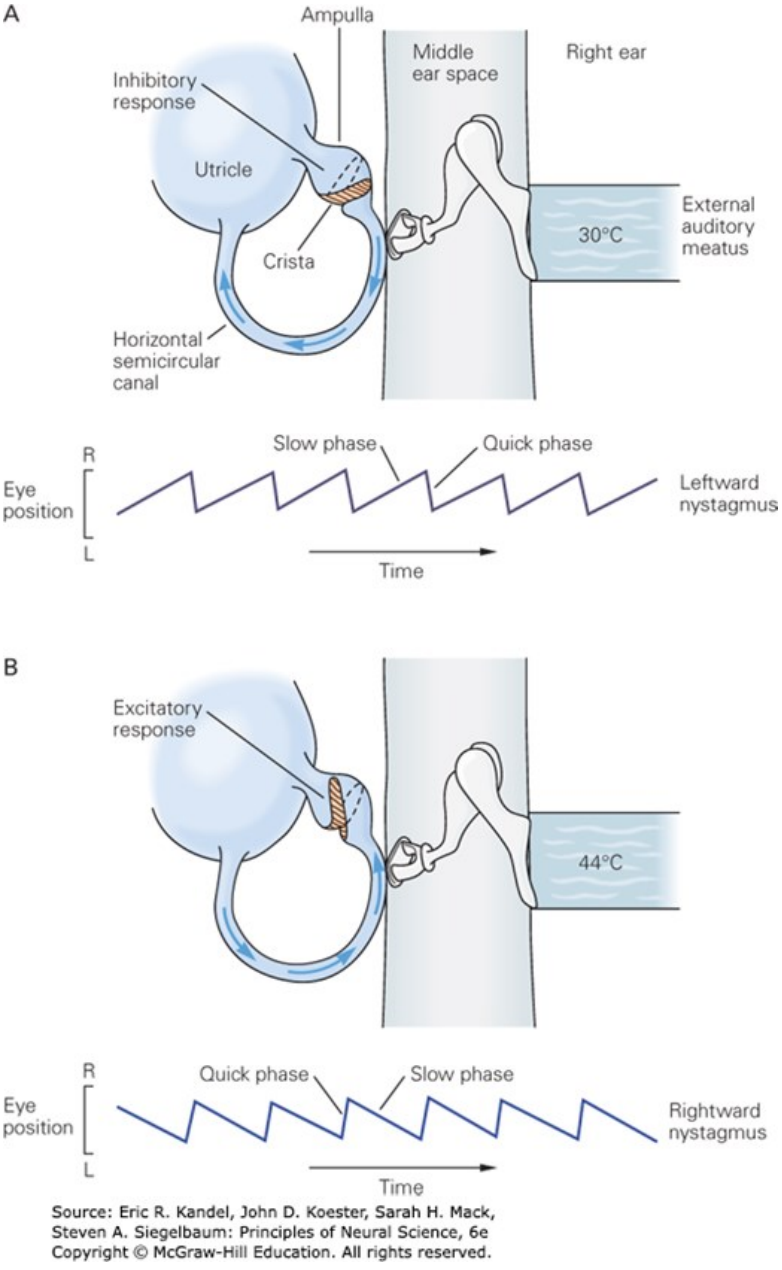
Nystagmus can be used as a diagnostic indicator of vestibular system integrity. In patients complaining of dizziness or vertigo, the function of the vestibular labyrinth is typically assessed by a caloric test (Figure 27–15). Either warm (44°C) or cold (30°C) water is introduced into the external auditory canal. In normal persons, warm water induces nystagmus that beats toward the ear into which the water has been introduced, whereas cold water induces nystagmus that beats away from the ear into which the water has been introduced. This relationship is encapsulated in the mnemonic COWS: **C**old water produces nystagmus beating to the **O**pposite side; **W**arm water produces nystagmus beating to the **S**ame side. In normal persons, the two ears give equal responses. If there is a unilateral lesion in the vestibular pathway, however, nystagmus will be induced and directed toward the side opposite the lesion.

Figure 27–15

Bithermal caloric test of the vestibulo-ocular reflex. The vestibular caloric test remains the primary test used today in clinics around the world to determine if there is system dysfunction. The head is elevated 30° to align the horizontal semicircular canals with gravity.

A. Cold water or air introduced into the right ear causes a downward convection current in the endolymph, producing an inhibitory response in the right ear hair cells and afferent fibers. The result is a leftward (opposite side) beating nystagmus (as determined by fast phase direction).

B. Warm water or air introduced into the right ear produces an upward endolymph movement, producing an excitatory response in the hair cells and afferents. The result is a rightward (same side) beating nystagmus.



The vertigo and nystagmus resulting from an acute vestibular lesion typically subside over several days, even if peripheral function does not recover. This is because central compensatory mechanisms restore the balance in vestibular signals in the brain stem, even when peripheral input is permanently lost or unbalanced.

The loss of input from one labyrinth also means that all vestibular reflexes must be driven by a single labyrinth. For the VOR, 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.

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 or cancer treatment medications such as cisplatin. The symptoms of bilateral vestibular hypofunction are different from those of unilateral loss. First, vertigo is absent 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.

In humans, receptor and nerve fiber loss due to disease, trauma, or ototoxicity is permanent. However, in other animal classes such as amphibians, reptiles, and birds, spontaneous regeneration does occur over time. Although the differences in regeneration between animal groups is not yet understood, recent research shows promise for the future development of regenerative treatments in humans.

For the present, 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 without steadying his head to keep it motionless. Even after partial recovery, he could not read 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 VOR fails to compensate for the miniscule head movements that accompany each arterial pulse.

Highlights

1. The vestibular system provides the brain with a rapid estimate of head movement. Vestibular signals are used for balance, visual stability, spatial orientation, movement planning, and motion perception.
2. Vestibular receptor hair cells are mechanotransducers that sense rotational and linear accelerations. Through kinematic and neural processing mechanisms, movements are transformed into acceleration, velocity, and position signals. These signals are used throughout the brain efficiently and quickly to guide behavior and cognition.
3. Receptor cells are polarized to detect the direction of motion. Three semicircular canals in each inner ear detect rotational motion and work in bilateral synergistic pairs through convergent commissural pathways in the vestibular nuclei. Two otolith organs in each ear detect linear translations and tilts relative to gravity.
4. Vestibular nuclei neurons receive converging multisensory and motor signals from visual, proprioceptive, cerebellar, and cortical sources. The multisensory integration allows for discrimination between active and passive body motion, as well as appropriate motor responses for reactive or volitional behavior.
5. Projections from the vestibular nuclei to the oculomotor system allow eye muscles to compensate for head movement through the vestibulo-ocular reflex to hold the image of the external world motionless on the retina. Cortical projections to the vestibular and oculomotor nuclei allow volitional eye movements to be separated from reflex eye movements but work through a final common pathway. Motor learning through vestibulocerebellar networks provides compensatory changes in eye movement responses to changing visual conditions through the use of spectacles, disease, or aging.
6. Projections from the vestibular nuclei to motor areas and the spinal cord facilitate postural stability. Gaze stability coordinates eye and neck movements through the medial vestibulospinal pathway. Postural control is exerted through the lateral vestibulospinal pathway.
7. Projections from the vestibular nuclei to the rostral and caudal medulla nuclei are involved in regulation of blood pressure, heart rate, respiration, bone remodeling, and homeostasis.
8. Projections from the vestibular nuclei to thalamus and cortex ensure spatial orientation and influence spatial perception more generally.
9. Vestibular signals processed in the hippocampal regions are crucial for spatial location and navigation functions.

10. Vestibular signals are combined with visual signals in several cortical regions through Bayesian cue integration to provide motion perception.

11. Disease or trauma to the vestibular system can produce nausea, vertigo, dizziness, balance disorders, visual instability, and spatial confusion.

12. We are only beginning to appreciate the role of the vestibular system in cognition. However, it is clear that vestibular signals contribute to our perception of self, conception of body presence, and memory.

13. New approaches in computation and theory promise to provide the lapidary keys needed to unlock our understanding of how vestibular signals contribute to the essence of brain function.

J. David Dickman

Dora Angelaki

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