THE VESTIBULAR SYSTEM

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LEARNING OBJECTIVES

- 1. Learn how the structures of the otolithic organs sense linear accelerations and how those organs in the two ears function as mirror-opposite pairs.
- 2. Learn how the semicircular canals sense angular accelerations of the head, how the horizontal semicircular canals function as complementary bilateral pairs to control eye movements so as to compensate for head rotation in the horizontal plane.
- 3. Learn how the major elements of the vestibular pathways, including the peripheral sensory organs, the primary afferent projections to the vestibular nuclear complex, the vestibulo-spinal pathways, the interactions with the cerebellum, and some elements of the vestibulo-ocular reflex pathways function to stabilize gaze and contribute to postural stability and our sense of body position.
- 4. Begin to learn about balance disorders, vestibular compensation, and clinical tests that can be used to assess the functional status of the vestibular system.

REFERENCES: Chapter 14 in Purves et al. *Neuroscience*, 4th edition.

OVERVIEW

For the most part our vestibular sensory system operates in the background, infrequently coming to the attention of our conscious mind, and yet the function of this system can be critical to normal quality of life. By age 75, dizziness and imbalance become the most common reason for patients to seek help from physicians. "Dizziness" is the most frequent symptomatic complaint of patients who experience vestibular system disorders, but the diagnosis of dizzy patients is challenging. Many cases of dizziness result from causes other than vestibular dysfunction. This lecture and next will provide you with the conceptual background for approaching the diagnosis of those patients.

Unconscious repositioning of our eyes rapidly compensates for both active and passive movements of the head, so that visual gaze is stable. Eye movements involved in that repositioning are controlled by the Vestibulo-Ocular Reflex (VOR) and important elements of neurological assessments. The vestibular system also makes important contributions to postural stability as well as to our sense of the body's position in space. Today's lecture will cover six topics: 1. vestibular system dysfunctions, 2. otolithic organ structures and functions, 3. how semicircular canals detect head rotation and control gaze stability, 4. structure and functions of vestibular centers and pathways of the brain, 5. tests of vestibular function, and 6. a highly adaptive, clinically important form of neural plasticity called vestibular compensation.

Dizziness and Balance Disorders:

- Dizziness, postural instability, and lack of stability during locomotion can all originate from dysfunctions in the vestibular system, but those symptoms are sometimes caused by other conditions in a patient who has normal vestibular function.
- Fluctuations in blood pressure, visual system abnormalities, and peripheral neuropathies all can lead to feelings of instability, lightheadedness, or imbalance.
- For that reason it is important to take an accurate patient history.

- If a patient reports feeling as though the environment is spinning or feeling as though they are moving through space those are often, but not always, indications of vestibular system involvement.
- Even with an accurate history it is still difficult to diagnose the causes of dizziness.
- It is important to be aware that the vestibular hair cells are particularly vulnerable to aminoglycoside antibiotic toxicity. Once these cells have been lost, they are not replaced. Patients on *i.v.* aminoglycosides are at risk for bilateral chemical lesioning of their vestibular and auditory organs.
- The increasing incidence of resistant forms of tuberculosis appears to be putting more patients at risk for such antibiotic induced **ototoxicity**.

Vestibular Hair Cell Structure and Response

- There are five sensory epithelia in the vestibular portions of the inner ear.
- Auditory and vestibular hair cells are similar in their basic structures and functions. Both have polarized hair bundles, but vestibular hair cells retain the kinocilium throughout life.
- As in their auditory counterparts deflection of the bundle in the direction of its tall end (the end near the kinocilium) causes depolarization and increases release of neurotransmitter
- Deflection of the bundle in the opposite direction causes hyperpolarization of the hair cell and results in less frequent action potentials in the postsynaptic afferent neuron.
- Each human utricle contains ~33,000 hair cells, each saccule contains ~19,000 hair cells, and each of the six ampullae contains ~8,000 hair cells.



It seems likely that the same mechanisms for **mechano-electrical transduction** function in both auditory and vestibular hair cells, but the sensory organs that these hair cells reside in differ significantly in the range of frequencies to which they respond. The cochlea senses frequencies from 20 Hz to 20 kHz, but vestibular detectors must sense accelerations of the head that are much slower movements, and have much lower frequencies. (Frequencies for vestibular stimuli are expressed in cycles per second or Hertz, with 1 Hz = one complete rotation of the head or head and body.)



Regular maintained (**tonic**) firing of neural impulses (as illustrated above) is a notable property of one common type of afferent vestibular neuron, but some vestibular afferents respond with irregular trains of impulses and others with brief (**phasic**) bursts of impulses.



Otolithic Organ Structure and Function

Between the cochlea and the semicircular canal organs are two sac-like organs, the utricle and the saccule, which communicate with the endolymph-containing space of the cochlear duct via the ductus reuniens (a narrow tube that runs between the base of the cochlea and the saccule). When the head is erect, most of the utricle's hair cell sensory epithelium, termed a macula, is in the horizontal plane, whereas most of the saccule's sensory epithelium (its macula) is in a nearly vertical plane. Both organs are referred to as

otolithic detectors because the hair bundles in their sensory epithelia lie embedded in gelatinous acellular **otolithic "membranes"** beneath otolithic masses comprised of thousands of microscopic football-shaped crystals of calcium carbonate called **otoconia**.



The **Otolithic masses** in the **utricle** and the **saccule** and the **cupulae** in the horizontal, anterior, and posterior **semicircular canals** have important influences, because they help to transform head movements into forces that deflect the bundles of the hair cells



The movements of the otolithic masses are subject to gravity. When the otolithic masses are pulled away from their rest positions that deflects the hair bundles beneath the otolithic membranes. The deflection modifies the generation of neural impulses that the brain interprets to provide a sense of the head's position in relation to the direction of gravity. Otoconia have significant mass, so they also act as inertial elements. When the head is accelerated the otoconia lag behind so hair bundle deflections caused in those situations indicate linear accelerations of the head.



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Position of the saccular and utricular maculae. Arrows indicate the direction of hair cell polarization on each side of the striola. (From Barber, HO and Stockweil, CW: Manual of Electronystagmography. CV Mosby, St. Loius, 1976, with permission)

As the small arrows in the figure illustrate, the hair cells in the utricular and saccular maculae are distributed in a range of orientations. (The arrows point in the direction of forces that cause depolarization of those hair cells.) Also, the hair cells on the two sides of each macula's **striola** have opposite directions of hair bundle orientation. A deflection in nearly any direction will be detectable as a stimulus that can cause depolarization in some portion of the hair cell population in either organ. Therefore, we can detect a range of head orientations in relation to the pull of gravity. For left or right head tilts the otoliths in the two ears work as **push-pull pairs**.





Semicircular Canal Structure and Function

Each semicircular canal has a swelling, called the **ampulla**, which contains its own hair cell sensory epithelium, termed a **crista**. The crista forms part of the inner lining which covers a crest of tissue that protrudes into the expanded, endolymph-filled lumen of the ampulla. The bundles of the crista's hair cells project into that endolymph fluid and adhere to an acellular, gelatinous **cupula**. Like the acellular, gelatinous tectorial membrane in the cochlea and the acellular, gelatinous otolithic membranes in the utricle and the saccule, the cupula helps to



transform a physical stimulus into a deflection of the hair bundles beneath it. The cupula is positioned like a gate spanning the lumen of the ampulla and hinged at those hair cell bundles.



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The three semicircular canals (Horizontal, Anterior, and Posterior) are in perpendicular planes. Like the cochlear duct, the utricle, and the saccule, they are filled with endolymph. Each ampulla is innervated by neurons that connect to hair cells in the crista. The semicircular canals detect angular accelerations of the head (i.e., rotational movements).

Rostral



Posterior

Semicircular canal functions can be illustrated by considering the example of the horizontal semicircular canals on the two sides of the head. The **endolymph** in each semicircular canal has <u>inertia</u>, and it is <u>not</u> directly coupled to the movement of the head, because it is a fluid. Therefore, when the head is rotated to the left within the plane of the horizontal canal (i.e. when the head rotates counterclockwise in the view above), the inertial fluid in the canal tends to lag behind the movement of the head and the walls of the semicircular canals. In effect, when the head rotates the fluid's inertia tends to make it stay put, so the walls of the canal (which are, of course, integral parts of the head) <u>initially move with the head around the inertially lagging endolymphatic fluid</u>.

As noted earlier, the cupula is positioned like a gate that is hinged by attachment to the hair bundles in the crista. The gate-like cupula projects across the endolymph fluid in the ampulla.

If we consider the left horizontal canal in the illustration above, we see that when the head is rotated to the left <u>the lagging inertial mass of fluid inside the canal</u> tends to push the cupula to the right, toward the rostral end of that semicircular canal. The force on the cupula thereby deflects the hair bundles in the crista in the direction of the <u>relative</u> fluid motion in the canal. The fluid in the right ear's horizontal canal also lags behind the leftward rotation of the canal walls, causing the right canal's cupula to be deflected away from the rostral end of its ampulla because of the mirror symmetry of the left and right canals.

How are the relative motions between the fluid and the canal walls sensed?

In both the left and the right horizontal canal ampullae, **all** the hair cells are oriented so that they will be depolarized by deflection of the cupula **directed toward the rostral end of the ampulla**. They are hyperpolarized by deflection of the cupula away from the rostral end. Because the right and the left horizontal canal cristae are "mirror opposites" of each other they always have opposing ("**push-pull**") responses to <u>horizontal</u> rotations of the head. Rapid

rotation of the head toward the left causes depolarization of hair cells in the left horizontal canal's ampulla and increased firing of action potentials in the neurons that innervate the left horizontal canal. That same leftward rotation of the head simultaneously causes a hyperpolarization of the hair cells in the right horizontal canal's ampulla and a decrease in the rate of firing of action potentials in the neurons that innervate the horizontal canal of the right ear.



As illustrated in the figure below, the vertical semicircular ducts from the two labyrinths send two signals to the brain resulting from the angular acceleration of the head in the plane of those ducts. The <u>right anterior</u> canal and the <u>left posterior</u> canal function together (as one "push-pull" pair), as do the left anterior and the right posterior canals.



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Central Vestibular Pathways

Primary vestibular projections: The cell bodies of the bipolar afferent neurons that innervate the hair cells in the maculae and cristae in the vestibular labyrinth reside near the **internal auditory meatus** in the **vestibular ganglion** (also called **Scarpa's ganglion**). The centrally projecting axons from the vestibular ganglion come together with axons projecting from the auditory neurons to form the eighth nerve, which runs through the internal auditory meatus together with the facial nerve. The primary afferent vestibular neurons project to four nuclei that comprise the **vestibular nuclear complex** (in the floor of the medulla beneath the fourth ventricle). The four nuclei of the vestibular nuclear complex are the lateral vestibular nucleus (also called Deiter's nucleus), the medial vestibular nucleus, the superior vestibular nucleus, and the inferior vestibular nucleus.

The lateral vestibular nucleus (or Deiter's nucleus) receives inputs from the utricle and the semicircular canals. It plays an important role in the maintenance of posture. Its second-order neurons send axons through the lateral vestibulospinal tract down to the ipsilateral ventral horn of the spinal cord. The tonic activation of those neurons has facilitatory effects on the alpha and gamma motor neurons that innervate the gravity-opposing muscles of the limb.

Normally the **cerebellar vermis** and higher centers contribute inhibitory projections to the lateral vestibular nucleus to counterbalance its excitatory influence on





those muscles. But in a patient whose brainstem has been transected above the level of the lateral vestibular nucleus, unmodified excitatory influences of the Deiter's nucleus projections (to the motor neurons that innervate the antigravity muscles) contributes to decerebrate rigidity in the limbs.

2) Both the medial vestibular nucleus and 3) the superior vestibular nucleus receive inputs primarily from the semicircular canals. The neurons in the medial vestibular nucleus make monosynaptic connections with motor neurons in the cervical spinal cord that innervate the muscles of the neck. Those connections are important in mediating reflex movements of the neck that tend to stabilize the position of the head in space.

Other neurons in the medial vestibular nucleus and the neurons of the superior vestibular nucleus participate in controlling the **vestibulo-ocular reflexes (VOR)**. Relatively large diameter axons from those cells ascend through the brainstem in a fiber bundle called the **medial longitudinal fasciculus**, (often simply referred to as the "**MLF**"). The MLF of each side of the brain lies just beneath the floor of the ventricle, near the midline. Fibers from vestibular nuclei that inhibit alpha motor neurons run in the portion of the MLF that descends through the spinal cord. The MLF is a useful landmark in brain sections and it's crucial for normal visual motor function.

4) The **inferior vestibular nucleus** receives inputs from the three semicircular canals, the saccule, the utricle, and the vermis of the cerebellum. This nucleus appears to be a site where vestibular inputs are integrated with inputs from other sensory systems and inputs from the cerebellum. It projects into the vestibulospinal and vestibuloreticular pathways.

Nucleus		Inputs	Outputs	Function/Interactions
1.	The Lateral Vestibular Nucleus (Deiter's Nucleus)	Utricles and Semicircular Canals	Project ipsilaterally via the lateral vestibulospinal tract	Facilitate activity of ventral horn alpha & gamma motor neurons that innervate gravity- opposing muscles of the limb for maintenance of posture
2.	The Medial Vestibular Nucleus and	Primarily from the Semicircular canals	MVN neurons make monosynaptic connections with	MVN neurons to cervical cord function in stabilizing the head in space.
and			cervical motor neurons that innervate neck	Ascending fibers in the MLF
3.	The Superior Vestibular		muscles.	give rise to the VOR by synapsing in the III, IV, and VI nerve nuclei. Descending fibers in the MLF project to the ventral horn at many levels (ipsilaterally at spinal levels) to synapse on alpha motor neurons and inhibit them.
			Other neurons in the MVN & the SVN send large diameter axons into the MLF (ascending and descending).	
4.	The Inferior Vestibular Nucleus	Semicircular canals, Utricles, Saccules, and Cerebellar Vermis	Project into the vestibulospinal and vestibuloreticular pathways.	Functions in integration of vestibular, multisensory, and cerebellar inputs.



Vestibular Function

The Vestibulo-Ocular Reflex Pathways:



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The **Vestibulo-Ocular Reflex (VOR)** results in movements of the eyes that are timed to coordinate with the movement of the head, so that the fovea can maintain its gaze on whatever target it is imaging. The <u>horizontal</u> VOR pathway coordinates the action of four muscles (the left and right lateral recti and the left and right medial recti) to stabilize visual gaze when the head is rotated in the plane of the horizontal semicircular canals. The basic pathway for the horizontal VOR is a three-neuron arc. <u>The first neurons are the afferent vestibular neurons</u> that project to the medial and superior vestibular nuclei. <u>The **second** neurons reside in those nuclei and project to the abducens nuclei and the oculomotor nuclei</u> that innervate the oculomotor muscles.

A **nystagmus** is an involuntary, <u>rythmic alternation of slow and fast-phase eye movements</u> that can be important in neurological diagnosis. The eye movements can be horizontal, vertical, rotational, or a mixture of those. In a <u>vestibular nystagmus</u> the eyes move slowly in one direction (so that gaze is stabilized) and then quickly move back in the opposite direction (so that the system in "reset" and a new region of gaze can be stabilized on the retina during the next slow-phase movement of the eyes). <u>By clinical convention</u> nystagmus is named for the direction of its fast phase.

Diagnosis via Caloric Testing

In the clinic, VOR function also can be assessed by **caloric tests**. For caloric testing the patient is put into a reclining position with a pillow propping the head up at a 30° angle. That brings the horizontal semicircular canals into a vertical plane aligned with the pull of gravity.

Then either cold or warm water is infused into one ear to induce convection that causes movement of the fluid that is within that ear's horizontal semicircular canal. Convectional flow effectively <u>simulates</u> the relative fluid movements that are normally induced by head rotation.

By causing convectional fluid movements in one ear, caloric testing produces an imbalance between the two ears in regard to the amount of neural impulses that propogate from each ear to the brain.

Normal patients will exhibit vestibular nystagmus during a caloric test. The normal **fastphase direction** of eye movements can be remembered using the mnemonic "C.O.W.S."



Fast phase direction of the nystagmus = C.O.W.S. = Cold-Opposite, Warm-Same

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The chapter in Purves et al. explains how you can use caloric testing to diagnose the status of the brainstem in unconscious patients. (*But it does not seem to give sufficient emphasis to a crucial point:* To understand the figure below from the Purves et al. book it's important to know that <u>the fast phase of nystagmus does</u> <u>not occur in patients who are unconscious</u>. For that reason, panels 3 and panel 4 of the book figure below show only the slow phase deviations for the unconscious patients.)



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Diagnosis of vestibular and eye-movement disorders can be aided by a number of objective measures. For instance, the alternating slow-phase and fast-phase movements of the eyes can be monitored electrophysiologically as the **electronystagmogram (ENG)** or via infrared imaging and computer tracking.

During the lecture on eye movements, the VOR pathways will be covered in greater detail. For our purposes it is worth noting that the VOR is remarkably plastic. The gain of the reflex changes in response to changes in the visual system, such as changes in the magnifying power of eyeglasses.

(Experiments conducted by G. Melville-Jones demonstrated that the direction of the reflex movements of the eyes would even reverse in volunteers who constantly wore prisms that reversed their visual image of the world. Fortunately it changed back to normal soon after the prisms were removed!)

Labyrinthectomy

Skull fractures that pass through the internal auditory meatus can crush or sever the eighth nerve and thereby result in a rapid unilateral removal of the neural impulses coming to the brain from one labyrinth. The **spontaneous nystagmus** that results from such a rapid unilateral labyrinthectomy has a slow-phase eye movement directed toward the side of the lesion and a fast-phase eye movement directed toward the intact side. (Think about the the eye movements that are controlled by the horizontal semicircular canals to understand why that would be the case.)

Such a rapid loss of inputs from one labyrinth can result in severe acute symptoms, which can include extreme dizziness, nausea, vomiting, deviation toward the side of the lesion when walking (if forced to walk a little), and that brisk spontaneous nystagmus, which interferes with vision.

In general, the magnitude of symptoms caused by labyrinthectomy depends on whether the loss is bilateral or unilateral, as well as the rapidity of the loss.

Patients who have experienced a slow-onset loss of vestibular function bilaterally, for example, as the result of aminoglycoside antibiotic toxicity, may not complain of symptoms related to vestibular function. However, their loss of normal vestibulo-ocular reflexes and vestibulo-spinal reflexes will result in oscillopsia (an oscillating instability of eyes) with head movements and instability when walking in the dark. (It's reported that those patients are resistant to seasickness.)

Vestibular Compensation

Fortunately recovery from unilateral labyrinthine loss occurs via **vestibular** compensation that begins almost immediately.

Within one week, a young patient may be able to walk without difficulty and may be able to suppress the spontaneous nystagmus.

After one month, most patients have few residual symptoms, but older patients may not recover as well.

Symptoms may return when patients have a cold or are ill in other ways.

The basis for vestibular compensation appears to be a learned modification in the brain's processing of signals that lead to reflexes, so that the unbalanced inputs from the vestibular system are ignored and the normal visual and proprioceptive inputs are relied upon exclusively.