Published in final edited form as:

Semin Hear. 2009 ; 30(4): 231–241. doi:10.1055/s-0029-1241124.

Anatomical and Physiological Considerations in Vestibular Dysfunction and Compensation

Sherri M. Jones, PhD [Associate Professor],

Department of Communication Sciences and Disorders, East Carolina University

Timothy A. Jones, PhD [Professor],

Department of Communication Sciences and Disorders, East Carolina University

Kristal N. Mills, BS [Doctoral Student], and

Department of Communication Sciences and Disorders, East Carolina University

G. Christopher Gaines, BS [Doctoral Student]

Department of Communication Sciences and Disorders, East Carolina University

Abstract

Sensory information from the vestibular, visual, and somatosensory/proprioceptive systems are integrated in the brain in complex ways to produce a final motor output to muscle groups for maintaining gaze, head and body posture, and controlling static and dynamic balance. The balance system is complex, which can make differential diagnosis of dizziness quite challenging. On the other hand, this complex system is organized anatomically in a variety of pathways and some of these pathways have been well studied. The vestibulo-ocular reflex (VOR) is one such pathway. Understanding the anatomy and physiology of the VOR facilitates our understanding of normal and abnormal eye movements and research is advancing our understanding of the plasticity of the vestibular system. This review highlights anatomical and physiological features of the normal vestibular system, applies these concepts to explain some clinical findings in some common peripheral vestibular disorders, and discusses some of the research investigating the anatomical and physiological basis for vestibular compensation.

Keywords

vestibular; anatomy; physiology; dysfunction; compensation; vestibular nuclei; cerebellum

Learning Objectives

1. The learner will be able to identify three functional pathways of the vestibular system and list key anatomical components for each.
2. The learner will be able to describe the anatomical and physiological basis for abnormal eye movements in unilateral vestibular dysfunction and BPPV.
3. The learner will be able to define static and dynamic vestibular compensation and identify key anatomical structures involved in each.

Introduction

Three sensory systems, vestibular, visual, and somatosensory/proprioceptive, serve our sense of balance. Each of these systems provides unique sensory information to the brain where it is integrated (often in complex ways) to produce a final motor output to muscle groups for maintaining gaze, head and body posture, and controlling static and dynamic balance. When one or more components of the balance system are affected, dizziness may result. The balance system is complex, which can make differential diagnosis of dizziness quite challenging. On the other hand, this complex system is organized anatomically in a variety of pathways and the physiology for some of these pathways is well understood.

Vestibular sensory input is used by the brain for several purposes including compensatory movements of the eyes to maintain gaze on visual targets or postural adjustments of the head and/or body that maintain balance during head movements. Other systems that maintain normal body functions may benefit from vestibular sensory input as well including those associated with thermoregulation, circadian rhythms and cardiovascular control^{1–3}. Clinically, we assess eye movements and static or dynamic postures in order to make inferences about the functional status of the vestibular sensors. Knowledge of the anatomy and physiology of vestibular pathways facilitates our understanding of eye movements and balance behaviors, enhances our ability to interpret test results, and explains various aspects of dysfunction as well as the brain's capability to compensate for vestibular deficits. Such knowledge helps us better understand dizzy or balance impaired patients and why their symptoms may change with time or with therapeutic intervention. This review highlights general vestibular anatomy and physiology, addresses some anatomical and physiological changes that occur with vestibular dysfunction, and discusses some of the neural mechanisms that may contribute to vestibular compensation.

Peripheral Vestibular Anatomy and Physiology

Several excellent reviews on vestibular anatomy and physiology are available^{4–12}. We briefly highlight some important features below. The reader is referred to the references for more detail.

The mammalian peripheral vestibular system consists of five end organs housed within the labyrinth of the inner ear and the vestibular portion of the eighth cranial nerve (Scarpa's ganglion). The vestibular labyrinth is a complex of fluid filled channels in the temporal bone that form the bony walls of the semicircular canals and the vestibule. The bony labyrinth is filled with perilymph. The membranous labyrinth is an extensive closed compartment within the bony labyrinth that is filled with endolymph and contains the neuroepithelia of the five vestibular end organs; three cristae contained in the ampullae of the semicircular canals and two maculae housed in the vestibule. Vestibular neuroepithelia are comprised of non-neural sensory receptor cells (hair cells), supporting cells, and the dendrites of vestibular primary afferent neurons. Specialized membranes are also associated with the cristae and maculae. Receptors of the cristae are covered by cupular membranes; whereas the receptors of the maculae are covered by otoconial membranes. The vestibular neuroepithelia encode information about movement and orientation of the head in space. The macular organs encode gravitational forces and linear acceleration, while the semicircular canals encode angular acceleration.

Vestibular hair cells are mechanoreceptors that have stereociliary bundles comprised of one kinocilium and multiple rows of stereocilia, all of which are embedded in the specialized membranes overlying the hair cells. Movement or shearing of the stereociliary bundle is critical for sensory transduction. Stimulation that produces a shearing motion of the bundle toward the kinocilium results in depolarization of the hair cells, release of neurotransmitter from the base of the hair cell, and increased neural discharge in the primary afferent neurons. Movement of

the stereociliary bundle away from the kinocilium results in hyperpolarization of hair cells, reduced neurotransmitter release, and decreased neural firing. Increased or decreased neural activity in the vestibular primary afferents is possible because these afferents are spontaneously active.

The orientation of the end organs in the head as well as the orientation of the stereociliary bundles enables the ampullae and maculae to encode head position or motion in any direction. For example, the anterior and posterior canals are oriented vertically at right angles to each other and the horizontal canal is oriented horizontally at approximately 30° above the horizontal plane. The stereociliary bundles within each crista are polarized such that the kinocilia are facing the same direction relative to the vestibule (or utricle specifically). In the anterior and posterior canals, the kinocilia and stereociliary bundles are oriented away from the utricle. In the horizontal canal the kinocilia are oriented toward the utricle. The multi-plane orientations of the canals along with the polarization vectors for each neuroepithelium are the basis for the directional sensitivity of the semicircular canals. The macular organs within each inner ear also are oriented in specific planes but have a more complex polarization pattern than the cristae. The saccule is oriented in a predominantly vertical position, while the utricle is predominately horizontal in orientation. When the head is in the upright, neutral position, saccular and utricular hair cells are most sensitive to movement primarily in the vertical and horizontal planes, respectively. However, complexity of the macular polarization vectors enables them to transduce linear head motion in any direction. The sensory areas of the utricle and saccule contain a distinctive central zone known as the striola. The stereociliary bundles on the two sides of the striola are oriented so that the kinocilia point in opposite directions. The result of this complex polarization pattern is that displacement of the otoconial membrane in any direction results in excitation of a subset of hair cells and inhibitory response in another subset. Furthermore, due to the curvature of the striola, polarization vectors change across the epithelia enabling a given end organ to respond to stimuli in multiple directions.

One other important feature of the periphery is that the end organs work together between the two ears. The semicircular canals are aligned in pairs across the head such that the two horizontal canals lie in a plane, while the anterior canal on one side is paired in a plane with the posterior canal on the contralateral side. The utricles and saccules are also paired across the head. Each pair of end organs works together in a complementary way to signal head motion to the brain. When head motion activates the end organ (or sensory patch in the case of the maculae) on one side of the head, its paired organ (or macular segment) on the opposite side is inhibited. Every head movement then stimulates a pair of vestibular organs. The paired action of the peripheral organs is critical for normal motor control of the eyes and postural muscles as well as normal perception. When one member of the pair is dysfunctional, inappropriate or inaccurate signals are transmitted to the brain. We will examine this physiology further for the vestibulo-ocular reflex pathway.

Central Vestibular Anatomy and Physiology

The central vestibular system consists of several relay nuclei and pathways coursing through various levels of the neuraxis. A simplified schematic of some of these relays is presented in figure 1. The vestibular primary afferents enter the brainstem at the pontomedullary junction; the majority of which synapse in the vestibular nuclear complex. Some vestibular afferents, however, have collaterals that synapse directly in the cerebellum.

The vestibular nuclear complex (VNC) consists of the vestibular nuclei and several nearby cell groups. The vestibular nuclei include four divisions: superior, lateral, medial and inferior and the nearby cell groups include the nucleus prepositus hypoglossi, cell group Y and cell group E. Each region of the VNC has some distinct afferent and efferent anatomical projections as well as some unique functional responsibilities. However, overall the VNC is a site for neural

integration of information from multiple sensory, motor and higher level cognitive systems. This complex integration produces appropriate output commands for control of eye, head, and body movements as well as output that may be critical for autonomic and cardiovascular control^{3,13,14}, attention and cognition^{15–17} as well as learning and memory^{18,19}.

The cerebellum plays a major functional role in motor coordination. It has three functional divisions, one of which is intimately involved with the vestibular system, namely the vestibulocerebellum. The vestibulocerebellar pathways include the flocculus, nodulus, vermis and fastigial nucleus. In addition to coordinating movements of the head and eyes, the vestibulocerebellum likely plays important roles in motor learning, adaptation¹⁸, and compensation from vestibular deficits (discussed below).

In general, the vestibular pathways that leave the VNC can be functionally categorized. Pathways to the thalamus and cortex serve sensation and perception of head motion. Vestibulospinal pathways provide motor commands to the muscles of the neck, upper torso and lower limbs to maintain balance and posture reflexively. The motor cortices projecting to the VNC, with the assistance of the cerebellum, can modulate the vestibulospinal output for smooth, well coordinated volitional movements or higher level reflexes. Pathways to the ocular motor nuclei and ultimately the muscles of the eye control compensatory eye movements during head motion (also known as the vestibulo-ocular reflex). Pathways also exist between the VNC and a variety of nuclei associated with the visual scene that are themselves critical for oculomotor functions of gaze, saccades, smooth pursuit and optokinetic nystagmus. These “visual scene” nuclei are distributed throughout the brainstem and include the superior colliculus, interstitial nucleus of Cajal, nucleus of the optic tract, accessory optic nuclei, inferior olivary nucleus as well as the prepositus hypoglossi. Communication between the VNC and visual scene nuclei allows for visual-vestibular interaction. The flocculus and vermis of the cerebellum also play a role in visual vestibular interactions.

Vestibulo-Ocular Reflex (VOR)

The vestibulo-ocular reflex (VOR) functions to maintain a steady image on the retina when the head is moving. It is quite effective for high frequency head movements. For example, when you walk or jog down the street, you still see the world clearly, can read the street signs and the house numbers in the neighborhood, because of the normal function of the VOR. One can simply demonstrate to himself how well the VOR works by first moving your eyes only to track your own finger that you are moving slowly in front of your face at arm’s length. As you increase the speed with which you move your finger in your visual field, you will see that the image of your finger blurs when you have exceeded the pursuit capability of your oculomotor system. Now hold your finger still and turn your head from side to side. If the VOR is functioning normally, you will see your finger clearly even as you increase the frequency of your head motion. The VOR produces compensatory eye movements that are opposite in direction to head movement to maintain a steady visual image. When the head turns to the right, the eyes move to the left and vice versa. Indeed, head movement in any direction produces an eye movement in the opposite direction. How is this possible? We use the horizontal VOR to illustrate the functional circuitry (also see figure 2). Horizontal movements of the eyes are controlled by two sets of muscles: the lateral rectus which moves the eye laterally or away from the nose, and the medial rectus which pulls the eye towards the nose. These muscles work in pairs to move the eyes conjugately (in the same direction) or disconjugately (in opposite directions). Conjugate eye movements in the horizontal plane require that the lateral rectus muscle for one eye and the medial rectus for the other eye contract to pull both eyes to the right or left. Returning to the VOR circuitry, recall how the end organs are activated and how they work together across the head. When the head turns to the right, the following physiological events take place:

1. The horizontal cristae in the right and left ears are excited (+) and inhibited (−), respectively.
2. Primary afferents of cranial nerve VIII on the right side increase their discharge rate while primary afferents on the left side decrease neural firing. Therefore, the right VNC receives increased peripheral input and the left VNC receives decreased input from the periphery.
3. Increased peripheral input to the right VNC activates second order neurons, which activate oculomotor (III) neurons on the right side, and cross the midline to activate neurons at the left abducens (VI) nucleus. Reduced peripheral neural activity seen at the left VNC results in decreased activity at the left oculomotor nucleus and the right abducens nucleus.
4. Internuclear projections from the abducens to the oculomotor nuclei reinforce activation and inhibition of the right and left oculomotor nuclei, respectively.
5. Motor neurons from the left abducens nucleus activate the left lateral rectus muscle to pull the left eye to the left. Motor neurons from the right oculomotor nucleus (cranial nerve III) will contract the medial rectus muscle of the right eye to pull this eye leftward. The lateral rectus of the right eye and the medial rectus of the left eye will relax since they have been disfacilitated (deactivated) by their respective motor nuclei (i.e., the right abducens and the left oculomotor nuclei).

While the primary purpose of the VOR is to maintain a stable visual image during head motion, the reflex pathway functions equally well without visual cues such that rotating the head in the dark also produces eye movement opposite to head movement. If the rotation is sustained, the slow movement of the eyes in one direction (slow phase) is followed by a quick movement of the eyes back to midline (quick phase). This pattern of slow and quick phases is known as induced nystagmus and it continues for several seconds during sustained rotation. Attenuation of the nystagmus with time is due primarily to fluid mechanics in the canal²⁰. Moreover, every pair of vestibular end organs has a VOR reflex pathway so compensatory eye movements can be evaluated for multiple directions and both angular and linear movements.

The VOR is actually a critical component of the vestibular test battery since it is activated during many assessment protocols including caloric irrigations, active and passive head movements, positioning tests such as the Dix-Hallpike maneuver, and several rotary chair tests. Indeed, as discussed below, spontaneous nystagmus due to unilateral vestibular dysfunction can be explained with VOR anatomy and physiology. The presence of a VOR, however normal or abnormal, serves as definitive evidence that vestibular receptors generate some neural activity that is transmitted to the brain because without such input, the VOR would be absent entirely. Moreover, the VOR can provide a means of quantifying abnormalities in the reflex arc and may be used in conjunction with other measures to localize disease to a particular ear or to a particular level of the neuraxis.

Vestibular Dysfunction

Deficits anywhere along the pathways discussed above can cause dizziness or imbalance. Numerous pathologies can affect these pathways; however, most pathologies can be broadly categorized as peripheral or central. Peripheral pathologies are those that affect the end organs in the inner ear and/or the eighth nerve. Central pathologies affect the pathways in the brain. The clinician who works with dizzy patients is well aware of the symptoms exhibited or expressed by patients with peripheral vestibular dysfunction including vertigo, nausea, vomiting, and exacerbation of symptoms with head movements. Indeed, peripheral pathologies in patients or experimental peripheral lesions in animal models have been well studied anatomically and physiologically. Therefore, we focus on peripheral pathologies and begin by

looking at VOR physiology in a selective inner ear disorder, benign paroxysmal positional vertigo (BPPV).

BPPV is one of the most common causes of vertigo that occurs when dislodged otoconia enter one of the semicircular canals. Some further distinguish the two pathological conditions of cupulolithiasis where dislodged otoconia are caught in the cupula, and canalolithiasis for debris floating within the semicircular canals; however, no distinction is needed for this discussion. The reader is referred to Herdman and Tusa for a historical perspective on this issue²². The debris increases the density of the cupula or displaces endolymphatic fluid which abnormally stimulates the affected cristae during benign (i.e., natural) head movements^{22, 23}. When the brain sees increased neural activity on one side relative to the other, it perceives that the head is moving and the VOR reflex circuit initiates compensatory eye movements. Clinically, BPPV patients present with episodic vertigo and nystagmus that subsides within seconds after onset. Because the onset of symptoms typically occurs with specific head movements, provocative maneuvers such as the Dix-Hallpike can be used to determine the presence of BPPV. However, knowledge of the VOR pathways allows one to determine which canal is most likely affected. If BPPV affected one of the horizontal semicircular canals, we would expect to see horizontal nystagmus with slow phases directed away from the affected ear and fast phases directed toward the affected side. Nystagmus is often described according to the direction of the fast phase so in this example the pathological nystagmus is beating toward the affected ear.

Horizontal BPPV is actually quite rare; Herdman and Tusa²¹ indicate its presence in only 5% of patients. Posterior canal BPPV is most common accounting for 75 to 95% of all cases of BPPV^{21, 24, 25} and the eye movements produced by posterior BPPV will be quite different than those produced by horizontal BPPV. The VOR pathways for the anterior and posterior semicircular canals differ from the horizontal VOR pathway in that different extraocular motor nuclei and different eye muscles are involved. Recall the paired functioning of the posterior canal of one ear with the anterior canal of the opposite ear. Activation of the posterior canal on one side is paired with inhibition of the anterior canal on the opposite side. Therefore, activation of the posterior canal on the right side, for example, would produce a compensatory eye movement that is leftward torsional (i.e., the superior pole of the eyes are rotated leftward) and down due to activation of the ipsilateral superior oblique muscle (via the trochlear nerve which is cranial nerve IV) and the contralateral inferior rectus (via cranial nerve III). The ipsilateral inferior oblique (via III) and the contralateral superior rectus (via III) muscles are deactivated in this example. Therefore, posterior canal BPPV produces a pathological nystagmus that beats upward and torsional toward the affected ear. Anterior canal BPPV, which is also quite rare, would produce nystagmus beating downward and torsional toward the affected ear.

While BPPV can be readily treated, many other unilateral peripheral deficits can be, and often are, permanent. Many causes underlie permanent unilateral peripheral dysfunction and the extent of the pathology can vary tremendously. Careful study of clinical patients and animal studies where one or more end organs have been selectively ablated or the vestibular nerve has been severed or silenced pharmacologically have provided the anatomical and physiological evidence to explain the clinical symptoms seen in permanent peripheral deficits. Curthoys and Halmagyi²⁶ nicely summarize the static and dynamic symptoms of unilateral vestibular deafferentation, which they abbreviate uVD. Static symptoms are present when the patient is not moving and include horizontal spontaneous nystagmus that suppresses with visual fixation, ocular tilt reaction and lateropulsion. When in the dark or with eyes closed, patients perceive that they are turning or rolling even though they are perfectly still. Dynamic symptoms require movement and include exacerbated perception of motion with head movements, abnormally slow velocity eye movements during head rotation, persistent asymmetry in the VOR when

comparing two directions of rotation, corrective saccades when moving the head at high accelerations, and abnormal ocular counter rolling.

What is the anatomical and physiological basis for some of the static and dynamic symptoms of uVD? Physiologically, the primary basis for most of the symptoms is an imbalance in the neural input to the VNC, which activates reflex pathways as if head motion were occurring. Let's use spontaneous nystagmus as one example. In uVD, the peripheral activity for one of the ears is silenced completely; however the intact ear still fires spontaneously when the head is at rest (not moving). Spontaneous nystagmus is produced because the spontaneous neural discharge from the intact ear drives the VOR pathway to produce compensatory eye movements away from the intact ear just as if the head had been rotated toward the intact ear. This generates pathological nystagmus that beats toward the intact ear or away from the lesioned ear. The VOR is functioning as expected when input from the two ears is different, but in this case, a difference in neural activity from the two ears is present even when the head is at rest. Often, but not always, the direction of spontaneous nystagmus can help the clinician predict which ear may be dysfunctional. Spontaneous nystagmus in uVD is suppressed with vision through the nuclei associated with the visual scene, which acting through a variety of pathways to the VNC ultimately relay information to the extraocular motor nuclei to stabilize gaze on the visible target. The abnormal vestibular information suggesting movement of the head is counteracted by the visual information demonstrating that the world is, in fact, stable.

The ocular tilt reaction is due to imbalance between the ears in terms of macular input. The head tilts away from the side with higher neural discharge (i.e., away from the intact ear). The body tilts away from the side with the higher neural discharge, and therefore the patient may lean toward the impaired ear (lateropulsion)²⁶.

While the clinician might appreciate the broad physiological changes occurring at the level of the VOR, numerous anatomical changes are occurring at the cellular level. For example, after surgical deafferentation, there is an eventual loss of vestibular axons and synapses at the VNC on the affected side²⁷, reduced numbers of cellular organelles responsible for protein synthesis (e.g., ribosomes and endoplasmic reticulum)²⁷, and the number of glial cells (non-neural supporting cells in the nervous system) increase in the VNC^{28,29}. Cellular changes in the brain due to peripheral dysfunction are not disputed; however it is important to note that the cellular changes described for deafferentation may not generalize to all cases of peripheral vestibular dysfunction.

Vestibular Compensation

Despite the fact that the peripheral input to the brainstem may be permanently absent in uVD, the static and dynamic symptoms of uVD are not all permanent. Many of the static symptoms, such as spontaneous nystagmus, skew deviation, lateropulsion disappear or diminish significantly within days of the insult. Dynamic symptoms take longer to resolve and may demonstrate persistent abnormalities. Perceptions of vertigo and motion also improve dramatically within days after uVD and individuals do return to normal or near normal activities as time passes from uVD. The fact that symptoms subside, some measurable responses return to normal, and patients can recover normal daily activities suggests that some form of compensation is taking place. Cawthorne³⁰ and Cooksey³¹ noted in the 1940's that patients with unilateral vestibular dysfunction who exercised dealt with symptoms better and recovered faster than those patients who did not exercise. Dealing with symptoms and recovery of function are the goals for vestibular rehabilitation programs. If the peripheral deficit is permanent (i.e., no recovery of function at the primary afferent level), what are the neurophysiological correlates for compensation?

The vestibular pathways in the brain evidence substantial plasticity or capacity to change. The VOR of normal healthy subjects has been well studied in this regard (reviews^{18,29}). The velocity and timing of compensatory eye movements produced by head movements are constantly recalibrated based on input about the changing environment via vision and other senses as well as information already stored in the brain. The VNC and the cerebellum are two important structures mediating normal adjustments and serving major roles in vestibular compensation following peripheral injury^{18,32,33}.

One physiological compensation at the level of the VNC occurs soon after the primary afferents have been silenced by uVD. Smith and Curthoys^{34,35} and Ris et al.^{36,37} demonstrated that the initial silencing of primary afferents causes reduced neural discharge at the VNC on the lesioned side (as discussed previously in the generation of spontaneous nystagmus) as well as increased neural discharge in the contralateral VNC. Subsequently, within hours to days, VNC neural discharge on the lesioned side returns to normal or near normal levels re-establishing balanced activity between the two VNC. The return of balanced activity between the VNC is correlated with the resolution of static symptoms (e.g., spontaneous nystagmus) and reduced perceptions of motion.

Several anatomical mechanisms have been suggested for the physiological compensation just described. Recall that the VNC integrates information from multiple relays. One additional important feature not previously emphasized is that the VNC on either side of the brainstem communicate extensively through commissural connections. These commissural connections are largely inhibitory and may play a significant role in re-establishing balanced neural discharge between the VNC during compensation³⁸. Other synaptic influences may come from the cerebellum. Intrinsic mechanisms within the VNC itself have also been suggested including regulation of receptors and altered neuronal excitability as well as a variety of biochemical changes (see review by Darlington & Smith³³).

While the return of balanced neural activity at the VNC may facilitate resolution of the static symptoms of UVD; the dynamic response properties of these neurons remain abnormal and dynamic symptoms persist. Some of the dynamic symptoms are permanent such as VOR abnormalities for high acceleration impulses; however, some VOR responses do show improvement with time. Leigh and Zee³² suggest that resolution of dynamic symptoms requires visual input and the cerebellum may play a role in the processing of this visual information. Recently, Beraneck et al.³⁹ studied compensation after uVD in mutant mice lacking Purkinje cells in the cerebellum. They concluded that the cerebellum is critical for recovery of some dynamic VOR responses.

There is still a great deal yet to learn about compensatory mechanisms. Compensation is variable across individuals. Often only partial compensation may occur and some may never compensate for peripheral vestibular dysfunction. Future research may reveal predictors for compensation outcomes as well as improved therapies (behavioral and/or pharmaceutical) to promote compensation.

Summary

This review highlighted some of the anatomical and physiological considerations in normal and abnormal vestibular function as well the neural basis for vestibular compensation. The anatomy and physiology of the vestibular system is complex yet organized along functional pathways including perceptual, vestibulo-oculomotor, visual-vestibular interaction, and vestibulospinal. The VNC serves a major role in all of these functional components as it integrates information from multiple sources and demonstrates a great deal of plasticity. Knowledge of vestibular anatomy and physiology facilitates our understanding of normal and disordered vestibular function as well as processes that may underlie recovery from

dysfunction. Research may ultimately lead to more sensitive diagnostic tools to accurately assess vestibular function, determine the status of compensation, and advance therapeutic interventions to facilitate compensation.

Abbreviations

VNC	Vestibular Nuclear Complex
BPPV	Benign Paroxysmal Positional Vertigo
VOR	Vestibulo-ocular Reflex
HSC	Horizontal Semicircular Canal
uVD	unilateral Vestibular Deafferentation
LR	Lateral Rectus
MR	Medial Rectus

References

1. Fuller PM, Fuller CA. Genetic evidence for a neurovestibular influence on the mammalian circadian pacemaker. *J Bio Rhythms* 2006;21:177–184. [PubMed: 16731657]
2. Fuller PM, Jones TA, Jones SM, Fuller CA. Neurovestibular modulation of circadian and homeostatic regulation: Vestibulohypothalamic connection? *Proc Natl Acad Sci* 2002;99(24):15723–15728. [PubMed: 12434016]
3. Yates BJ, Bronstein AM. The effects of vestibular system lesions on autonomic regulation: Observations, mechanisms, and clinical implications. *J Vestib Res* 2005;15(3):199–129.
4. Asher, DL. Vestibular anatomy and physiology. In: Northern, JL., editor. *Hearing Disorders*. 2. Boston, MA: Little, Brown and Company; 1984. p. 195-204.
5. Buttner-Ennever, JA. Overview of the vestibular system: Anatomy. In: Beitz, AJ.; Anderson, JH., editors. *Neurochemistry of the Vestibular System*. Boca Raton, FL: CRC Press, LLC; 2000. p. 3-24.
6. Luxon, LM. The anatomy and physiology of the vestibular system. In: Dix, MR.; Hood, JD., editors. *Vertigo*. Chichester, UK: John Wiley & Sons, Ltd; 1984. p. 1-33.
7. Lysakowski, A.; McCrea, RA.; Tomlinson, RD. Anatomy of vestibular end organs and neural pathways. In: Cummings, CW., editor. *Otolaryngology- Head and Neck Surgery*. 2. St. Louis, MO: Mosby; 1993. p. 2525-2547.
8. Lysakowski, A.; Goldberg, JM. Morphophysiology of the vestibular periphery. In: Highstein, SM.; Fay, RR.; Popper, AN., editors. *The Vestibular System*. New York, NY: Springer-Verlag; 2004. p. 57-151.
9. Purves, D.; Augustine, GJ.; Fitzpatrick, et al. The vestibular system. In: Purves, D.; Augustine, GJ.; Fitzpatrick, D., et al., editors. *Neuroscience*. Sunderland, MA: Sinauer Associates, Inc; 2008. p. 343-362.
10. Schubert, MC.; Shepard, NT. Practical anatomy and physiology of the vestibular system. In: Jacobsen, GP.; Shepard, NT., editors. *Balance Function Assessment and Management*. San Diego, CA: Plural Publishing, Inc; 2008. p. 1-11.
11. Hain, TC.; Rudisill, H. Practical anatomy and physiology of the ocular motor system. In: Jacobsen, GP.; Shepard, NT., editors. *Balance Function Assessment and Management*. San Diego, CA: Plural Publishing, Inc; 2008. p. 13-26.
12. Highstein SM, Holstein GR. The anatomy of the vestibular nuclei. *Prog Brain Res* 2006;151:157–203. [PubMed: 16221589]
13. Carter JR, Ray CA. Sympathetic responses to vestibular activation in humans. *Am J Physiol Regul Integr Comp Physiol* 2008;294(3):R681–688. [PubMed: 18199586]
14. Balaban CD, Thayer JF. Neurological bases for balance-anxiety links. *J Anxiety Disord* 2001;15:53–79. [PubMed: 11388358]

15. Hanes DA, McCollum G. Cognitive-vestibular interactions: A review of patient difficulties and possible mechanisms. *J Vestib Res* 2006;16:75–91. [PubMed: 17312336]
16. Redfern MS, Talkowski ME, Jennings JR, Furman JM. Cognitive influences in postural control of patients with unilateral vestibular loss. *Gait Posture* 2004;19:105–114. [PubMed: 15013498]
17. Smith PF, Zheng Y, Horii A, Darlington CL. Does vestibular damage cause cognitive dysfunction in humans? *J Vestib Res* 2005;15:1–9. [PubMed: 15908735]
18. Gittis AH, duLac S. Intrinsic and synaptic plasticity in the vestibular system. *Curr Opin Neurobiol* 2006;16:385–390. [PubMed: 16842990]
19. Smith PF, Horii A, Russell N, Bilkey DK, Zheng Y, Liu P, Kerr DS, Darlington CL. The effects of vestibular lesions on hippocampal function in rats. *Prog Neurobiol* 2005;75:391–405. [PubMed: 15936135]
20. Rabbitt, RD.; Damiano, ER.; Grant, JW. Biomechanics of the semicircular canals and otolith organs. In: Highsten, SM.; Fay, RR.; Popper, AN., editors. *The Vestibular System*. New York, NY: Springer-Verlag; 2004. p. 153-201.
21. Herdman, SJ.; Tusa, RJ. Physical therapy management of benign positional vertigo. In: Herdman, SJ., editor. *Vestibular Rehabilitation*. Philadelphia, PA: FA Davis Co; 2000. p. 233-260.
22. Baloh, RW.; Honrubia, V. *Clinical Neurophysiology of the Vestibular System*. 2. Philadelphia, Pa: FA Davis Co; 1990.
23. Rajguru SM, Ifediba MA, Rabbitt RD. Biomechanics of horizontal canal benign paroxysmal positional vertigo. *J Vestib Res* 2005;15(4):203–214. [PubMed: 16286702]
24. Cakir BO, Ercan I, Cakir ZA, Civelek S, Sayin I, Turgut S. What is the true incidence of horizontal semicircular canal benign paroxysmal positional vertigo? *Otolaryngol Head Neck Surg* 2006;134(3): 451–454. [PubMed: 16500443]
25. Honrubia V, Baloh RW, Harris MR, Jacobson KM. Paroxysmal positional vertigo syndrome. *Amer J Otol* 1999;20(4):465–470. [PubMed: 10431888]
26. Curthoys, IS.; Halmagyi, M. Vestibular compensation: Clinical changes in vestibular function with time after unilateral vestibular loss. In: Herdman, SJ., editor. *Vestibular Rehabilitation*. Philadelphia, PA: FA Davis Co; 2000. p. 76-97.
27. Gacek RR, Schoonmaker JE. Morphologic changes in the vestibular nerves and nuclei after labyrinthectomy in the cat: A case for the neurotrophin hypothesis in vestibular compensation. *Acta Otolaryngol* 1997;117(2):244–249.
28. Campos Torres A, Vidal PP, deWaele C. Evidence for a microglial reaction within the vestibular and cochlear nuclei following inner ear lesion in the rat. *Neurosci* 1999;92:1475–1490.
29. deWaele C, Campos Torres A, Josset P, Vidal PP. Evidence for reactive astrocytes in rat vestibular and cochlear nuclei following unilateral inner ear lesion. *Eur J Neurosci* 1996;8:2006–2018. [PubMed: 8921291]
30. Cawthorne T. Vestibular injuries. *Proc Royal Soc Med* 1946;39:270–273.
31. Cooksey FS. Rehabilitation in vestibular injuries. *Proc Roy Soc Med* 1946;39:273–278. [PubMed: 19993269]
32. Leigh, RJ.; Zee, DS. *The Neurology of Eye Movements*. 4. New York, NY: Oxford University Press; 2006. p. 53-62.
33. Darlington CL, Smith PF. Molecular mechanisms of recovery from vestibular damage in mammals: Recent advances. *Prog Neurobiol* 2000;62:313–325. [PubMed: 10840152]
34. Smith PF, Curthoys IS. Neuronal activity in the contralateral medial vestibular nucleus of the guinea pig following unilateral labyrinthectomy. *Brain Res* 1988;444:295–307. [PubMed: 3359297]
35. Smith PF, Curthoys IS. Neuronal activity in the ipsilateral medial vestibular nucleus of the guinea pig following unilateral labyrinthectomy. *Brain Res* 1988;444:308–319. [PubMed: 3359298]
36. Ris L, Godaux E. Neuronal activity in the vestibular nuclei after contralateral or bilateral labyrinthectomy in the alert guinea pig. *J Neurophysiol* 1998;80:2352–2367. [PubMed: 9819248]
37. Ris L, DeWaele C, Serafin M, Vidal PP, Godaux E. Neuronal activity in the ipsilateral vestibular nucleus following unilateral labyrinthectomy in the alert guinea pig. *J Neurophysiol* 1995;74:2087–2099. [PubMed: 8592199]

38. Graham BP, Dutia MB. Cellular basis of vestibular compensation: Analysis and modeling of the role of the commissural inhibitory system. *Exp Brain Res* 2001;137:387–396. [PubMed: 11355384]
39. Beraneck M, McKee JL, Aleisa M, Cullen KE. Asymmetric recovery in cerebellar-deficient mice following unilateral labyrinthectomy. *J Neurophysiol* 2008;100(2):945–58. [PubMed: 18509072]
40. McElligott, JG.; Spencer, RF. Neuropharmacological aspects of the vestibule-ocular reflex. In: Beitz, AJ.; Anderson, JH., editors. *Neurochemistry of the Vestibular System*. Boca Raton, FL: CRC Press, LLC; 2000. p. 199-222.

Figure 1.

Simplified schematic of the central vestibular pathways. The flow of information between relays and across the midline is depicted by the arrows. For clarity, connections are only shown for the left side. Parallel pathways exist on both sides of the brain. Adapted from Lysakowski et al.⁷ and McElligott and Spencer⁴⁰.

Figure 2.

Schematic representation of the horizontal VOR from a dorsal perspective. The dashed line bisecting the figure represents the midline. Net excitation and inhibition (or deactivation) are indicated by the '+' and '-' signs, respectively. See text for details. HSC – Horizontal Semicircular Canal, VNC – Vestibular Nuclear Complex, VI – Abducens Nucleus, III – Oculomotor Nucleus, LR – Lateral Rectus, MR – Medial Rectus