

# **Paparella: Volume I: Basic Sciences and Related Principles**

## **Section 2: Physiology**

### **Part 1: Ear**

#### **Chapter 10: Peripheral Vestibular System**

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The peripheral vestibular system consists of the vestibular apparatus and its afferent and efferent neural innervation.

In each ear, the vestibular apparatus, or labyrinth, consists of a series of interconnected membranous sacs and tubes that are contained in the petrous portion of the temporal bone. These tubes and sacs form the three semicircular canals and two otolith organs that together occupy a space of about 1 cm<sup>3</sup>. The membranous labyrinth is filled with endolymph and, together with the cochlea and the endolymphatic sac, forms a closed, fluid-filled system. Perilymph surrounds the membranous labyrinth and, together with fibrous microfilaments, supports the membranous labyrinth within the bony labyrinth. The bony labyrinth, a shell, serves as an interface between the membranous vestibular apparatus and the hard temporal bone.

The semicircular canals and otolith organs are innervated by the superior and inferior divisions of the vestibular portion of the eighth cranial nerve.

#### **Orientation of the Peripheral Vestibular System**

The vestibular apparatus is located lateral and posterior to the cochlea in the inner ear. Its afferent innervation courses medially and exits intracranially through the internal auditory meatus. The cell bodies of the afferent bipolar cells, whose preganglionic fibers innervate the vestibular neuroepithelium and whose postganglionic fibers course to the brain stem and cerebellum, are contained in Scarpa's ganglion, inside the internal auditory meatus.

In each ear, there is a complementary set of vestibular structures, including one horizontal semicircular canal, two vertical (anterior and posterior) semicircular canals, and two otolith organs (utricle and saccule). The major plane of the horizontal semicircular canals lies in a plane that is inclined upward by an angle of approximately 30 degrees from the horizontal head plane. The two vertical semicircular canals lie in the vertical head plane, but are displaced 45 degrees from the midsagittal plane. The major plane of the anterior semicircular canal and the ipsilateral posterior semicircular canal are approximately 90 degrees from each other. The major plane of the anterior semicircular canal in one ear is coplanar with the major plane of the posterior semicircular canal in the contralateral ear. Since the major plane of the utricle is approximately in the same plane as the horizontal semicircular canal, its major plane also is inclined 30 degrees upward from the horizontal plane. The plane of the saccule is roughly orthogonal to the plane of the utricle, and approximately coplanar with the midsagittal plane. The orientation of the planes of the semicircular canals and otoliths in the head is important physiologically, since neural networks

in the brain must overcome the difference between the planes of these receptors and those of the extraocular, neck, and spinal muscles (effectors) to provide perfect compensation of the eyes, head and body in three-dimensional space (Pellionisz and Graf, 1987; Pellionisz and Llinas, 1977; and Pellionisz and Peterson, 1988).

### **Endolymph and Perilymph**

This distribution is meaningful because (1) the unusual ionic composition of the endolymph may play a role in the ionic currents associated with mechanoelectric transduction by the hair cells in the semicircular canals and otolith organs (Hudspeth, 1983); (2) the pressure homeostasis between the endolymph and perilymph may contribute to normal responses of the semicircular canals during caloric nystagmus (Scherer and Clarke, 1985; and Scherer et al, 1986), vertigo resulting from Ménière's disease (Dohlman, 1965; and Laurence and McCabe, 1959), and vertigo resulting from fistulae in the bony labyrinth (eg, alternobaric vertigo (Britton, 1986; Love and Correia, 1980; and Lundgren and Malm, 1976)).

The endolymph is an unusual extracellular fluid in that it has a high potassium (150 mM) and low sodium (16 mM) content. Perilymph, on the other hand, like cerebrospinal fluid, has a high sodium (150 mM) and low potassium (7 mM) content (Rauch and Koestlin, 1958). Endolymph circulates both focally and longitudinally in the vestibular apparatus (Dohlman, 1973). The longitudinal circulation involves secretion by specialized cells and excretion of cellular debris by the endolymphatic sac. The specialized secretory cells in the vestibular apparatus are found on the lower slopes of the cristae (Iwata, 1924) and in the planum semilunatum (Dohlman, 1973). The location of these regions is described in the next section. Focal circulation involves both secretion and pinocytosis or absorption by lysosomes in nonsensory cells of the labyrinth (Dohlman, 1973). In addition to circulation of organic material, circulation of ionic species apparently occurs in the labyrinth. Water and ions slowly diffuse from the perilymph into the endolymph (Rauch et al, 1963) and dark cells (specialized nonsensory cells that appear dark when stained and viewed with transmission electron microscopy) are involved in the removal of sodium and the pumping of potassium into the endolymph (Matchinsky and Thalmann, 1967). Typically, reconstituted endolymph bathes the surfaces of the neuroepithelia of the semicircular canals and otolith organs, while perilymph bathes the vestibular nerve and its branches. It is important that large concentrations of these fluids remain separate. If a relatively large amount of endolymph, with its high K<sup>+</sup> concentration, leaked into the perilymphatic space and mixed with the perilymph (as might occur following a rupture of the membranous labyrinth or displacement of the stapes footplate from the oval window), the vestibular and cochlear nerves might become transiently depolarized. This depolarization could, in turn, cause the action potential firing rate of the afferents to increase until some form of central compensation occurred or until homeostasis of the endolymph and perilymph fluids reoccurred (Dohlman, 1965).

### **Contents of the Ampullae and Maculae**

On each of the semicircular ducts there is an enlargement or swelling, the ampulla, that contains the sensory neuroepithelium. Hair cells and supporting cells are embedded in an epithelial layer that lies on a saddle-shaped ridge, the crista, that extends across the base of the ampulla at right angles to the membranous semicircular duct. At each end of the crista on the surface of the ampullary wall is a semicircular ridge of nonsensory cells that forms a

structure, the planum semilunatum. As pointed out in the last section, the planum semilunatum is thought to be one of the endolymph secretory areas. Extending from the top of the crista and attaching to the walls and roof of the ampulla is a gelatinous structure (mucopolysaccharides within a keratin meshwork), the cupula. The cupula forms a fluid-tight partition across the ampulla. The cilia arising from the apical ends of the hair cells, whose cell bodies are embedded in the crista, project into and are attached to the base of the cupula. The specific gravity and refractive index of the cupula are the same as that of the endolymph, which, in turn, is similar to that of water. The absence of a density difference between the cupula and the surrounding endolymph supposedly makes the cupula-endolymph system normally only respond to angular acceleration and not gravity. This dogma is still controversial (Goldberg and Fernandez, 1975; and Perachio and Correia, 1983). There is evidence that certain substances can modify the density relationship between the cupula and surrounding endolymph. For example, a positional nystagmus, which might be observed during an otoneurologic examination, could be caused by density differences between the cupula and endolymph resulting from prior alcohol ingestion (Money et al, 1965; Nito et al, 1964).

Structures analogous to the cristae, the maculae, are found within the utricle and saccule. Like the cristae, the maculae contain the sensory neuroepithelium (hair cells), supporting cells and capillary beds. In the otolith organs, however, the tips of hair cell cilia are embedded in the bottom of a gelatinous membrane (statoconorium or otoconial membrane) that does not extend across the otolith organ but forms a gelatinous coating over the maculae. Attached to the top surface of this membrane, like frosting on a cake, are calcium carbonate crystals (the otoconia) that, taken as a layer, form a mass that is about three times as dense as the surrounding endolymph. The density difference between the otoconial mass and the surrounding endolymph allow the otolith organs to act as gravity sensors. There is no evidence, obtained by recording from otolith afferents, that the otolith organs respond to angular acceleration.

The surface of the utricle and saccule, when viewed from above, are spade (escutcheon) and hooked-shaped, respectively. The surface of the calcite crystal frosting on the otoconial membrane is relatively uniform, with the exception of one distinctive region that courses along the long axis of the macula. This region is called the striola (Werner, 1933). In the utricle, a slight depression in the calcite crystal layer defines the striola; in the saccule, a mounded ridge of calcite crystals defines the striola. The striola is an important landmark because it serves as a dividing line for morphologic and physiologic polarization of hair cells (see the following section).

### **Morphologic and Physiologic Polarization of Hair Cells**

Viewed from above, a cross-section just above the apical surface of a typical hair cell shows 60 to 100 stereocilia, arranged in a hexagonal array, and one kinocilium. The stereocilia are like the much shorter microvilli that are found in neighboring supporting cells, and the kinocilium is a true cilium. When viewed from the side, the stereocilia are arranged in rows of ascending ranks like the pipes of a pipe organ. Since hair cells in the cochlea have only rudimentary kinocilia and since kinocilia of vestibular hair cells regress in some species without affecting transduction, it is believed that the stereocilia are responsible for mechanoelectric transduction. However, for vestibular hair cells, the kinocilium is the longest

and most eccentric of the cilia and, therefore, it can be considered as the tip of a pointer for referencing orientation of the cilia relative to other structures in the labyrinth and for indicating the direction of deflection of the stereocilia. Hair cells on either side of the striola have their kinocilia (represented in cartoon fashion as the tallest cilia) facing the striola (represented by a depression of overlying small crystals in the otolith layer). In both the utricle and the saccule, since the striola bisects the macula, hair cells on either side of the striola are arranged with opposing morphologic polarization (ie kinocilia point toward each other). Hair cells on the cristae of the semicircular canals are also morphologically polarized. However, since the cristae are relatively symmetric, homogeneous structures, the orientation of the kinocilia are generally referenced to the utricle. In the horizontal crista, the kinocilia of all of the hair cells in the crista point toward the part of the utricle closest to the ampulla. In the vertical canals, the kinocilia of all of the hair cells point away from the part of the utricle closest to the ampulla.

The importance of morphologic polarization of hair cells in the vestibular organs becomes apparent from the physiologic correlate. It can be inferred from earliest work (Wersall et al, 1965) that when the stereocilia are deflected toward the kinocilium, the membrane potential of the hair cell is depolarized relative to the resting potential (about -60 mV) and the firing rate on the vestibular primary afferent that innervates the hair cell increases relative to the resting spontaneous rate (about 90 impulses/sec). Conversely, when the stereocilia are deflected away from the kinocilium, the membrane potential of the hair cell is hyperpolarized relative to its resting membrane potential and the firing rate of action potentials on the vestibular primary afferents decrease relative to the resting firing rate. Thus, the vestibular afferent fibers are able to transmit the bidirectional sensitivity of a given hair cell by increases and decreases in firing rate relative to the spontaneous firing rate.

### **Mechanics of Semicircular Canal and Otolith Organ Function**

Each of the semicircular ducts, with its ampulla and the utricle, can be thought of simplistically as a circular, fluid-filled tube (toroid) of varying diameter (larger at the utricle and ampulla) with an internal partition, the cupula, across it at one spot. As described above, the kinocilia of the hair cells in both the left and right labyrinths are on the sides of the hair cells toward the part of the utricle closest to the ampulla. A hypothetical comparator is located in the vestibular nuclei and represented by a circle, divided into four quadrants, that senses the neural activity from the left and right horizontal semicircular canal nerves. General neural activity in the nerve is represented as a train of action potentials on a single, typical afferent in the panels at the bottom of the figure. When the head is stationary, spontaneous activity occurs in both the right and left vestibular nerves and the action potential firing frequency is equal. This is represented by the two pluses, in both the right and left quadrants of the comparator. However, when a rightward horizontal head movement is initiated, the semicircular duct that is attached to the skull rotates to the right, but the endolymph contained within the duct, because of its inertial properties, tends to remain fixed in space and lags behind the skull movement. In effect, this lag produces a relative movement between endolymph and duct wall. This movement of endolymph (presumed to be less than 10 microns) causes the cupula partition, in the right (*left*) ear, to be deflected toward (*away from*) the part of the utricle closest to the ampulla. The cupula deflection causes the stereocilia to deviate.

The firing frequency decreases in the left vestibular nerve but increases in the right vestibular nerve. This difference is indicated by an imbalance in the pluses in the left and right quadrants of the comparator. As the head decelerates near the end of the movement, the conditions reverse, and at the termination of the head movement, the neural activity returns to the spontaneous level. In the above example, as the head begins to turn to the right, the eyes slowly deviate to the left in the horizontal plane in order to maintain stable retinal images. This slow eye deviation continues until the head turn is so great that the eyes can no longer rotate; then they quickly return toward the center. This alternation of slow deviation and fast return corresponds to the slow and fast phases of nystagmus seen during large angles of head rotation. The slow deviation of the eyes is indicated in the top of the figure by small black arrows above the eyeballs. As the head turns to the right, the obvious sense of rotation of the head is to the right.

A similar diagram could be made for pitch head movements, by considering the anterior semicircular canal in one ear and the contralateral coplanar posterior semicircular canal in the contralateral ear.

Under certain conditions, the comparator within the central nervous system misinterprets the imbalance of neural activity on the vestibular nerves as a head turn and produces physiologically appropriate ocular and postural responses. However, since the head is not turning, these responses are actually inappropriate and result in spontaneous nystagmus, perception of the visual surrounding as spinning, and a tendency to fall. An ablative lesion in the left vestibular nerve causes decreased neural activity in the left vestibular nerve. An imbalance relative to the spontaneous discharge level in the right vestibular nerve occurs, and this imbalance is interpreted by the comparator as a head turn to the right. Since the imbalance persists, the comparator interprets this as continuous head acceleration to the right. Consequently, nystagmus, with slow deviation of the eyes to the left and fast phases to the right, ensues. Attempts to perform a tandem Romberg test, for example, would result in a tendency to fall to the left; that is, the postural motor response is in the same direction as the physiologic oculomotor response (slow phase of nystagmus).

Figure illustrates neural activity that would occur in the left and right horizontal semicircular canal nerves during cold, caloric irrigation of the left ear of a patient with normal function. During this test, the patient would be lying on his or her back with the horizontal semicircular canals oriented vertically. If one could view the horizontal semicircular canals through the top of the head and applied cold water to the external ear canal, the following chain of events could be imagined. As the cold water cooled successively the lateral parts of the external canal, the temporal bone, and the left semicircular canal, the endolymph would become more dense than that contained in the utricle or the more medial part of the semicircular duct. Gravity would tend to cause the more dense endolymph to fall and endolymph motion would occur in the left semicircular canal. The cupula would thus deflect away from the closest part of the utricle, producing a decrease in the discharge firing rate in the left vestibular nerve relative to the spontaneous discharge in the right vestibular nerve and the slow phase of nystagmus (and correspondingly, the oppositely directed fast phase) would be the same as that observed during the beginning of a head turn to the right or during a pathologic condition resulting from an ablative lesion in the left vestibular nerve. Warm irrigation of the external auditory meatus, through the chain of events described above, would cause the slug of endolymph in the lateral part of the semicircular canal to be less dense than

that in the medial part. The slug would tend to rise, and the reactions would be opposite to that observed for the cold caloric response.

The mechanisms just described provide a physiologic basis for responses seen in the clinic and vestibulo-ocular responses known to most otolaryngologists. One can predict that, generally, a peripheral ablative lesion in one ear will cause nystagmus to beat (fast phase will be directed) toward the opposite ear. Moreover, during caloric irrigation, the fast phase of nystagmus will beat away from the ear irrigated by cold water but toward the ear irrigated by warm water. That is, cold irrigation causes nystagmus to beat toward the opposite ear; warm irrigation causes nystagmus to beat toward the same ear (COWS). Finally, during a tandem Romberg test, there is a tendency for the patient with an acute ablative lesion to fall toward the side of the affected ear.

A similar simple diagram can be constructed for the utricle. The otolith organs function to sense the orientation of the head relative to gravity. These receptors are stimulated by linear acceleration and tilt of the head. Otolithic stimulation is thought to produce small, appropriate, compensatory eye movements to maintain a veridical perception of earth vertical and earth horizontal during pitch and roll head tilts. There is also evidence that under certain situations, stimulation of the otolith organs can produce nystagmus (Cohen et al, 1983; and Correia and Money, 1970).

When the head is tipped (rolled) to the left, the otoconial membrane of the right utricle moves medially, while the otoconial membrane of the left utricle moves laterally. The physics of the movement is like that of a mass on an inclined plane. Since the otoconial membrane is three times the density of the surrounding endolymph, the force of gravity causes the otoconial membrane containing the tips of the stereocilia to slide relative to the macula in which the bodies of hair cells are embedded. Thus, the stereocilia are sheared, and because of the morphologic and physiologic polarization discussed above, the hair cells in the right utricle that are on the lateral-most side of the striola would be depolarized and those that are on the medial part of the utricle would be hyperpolarized. The opposite conditions would occur in the left utricle. The otoconial membrane movements described above would reverse for left-sided head rolls. Vestibulo-ocular pathways, involving the otoliths and the extraocular muscles, evoke counter-rotation of the eyes to maintain the correct visual orientation of earth vertical and earth horizontal. Similarly, vestibulospinal pathways, involving the otolith organs and skeletal muscles, evoke postural responses to prohibit loss of balance. One could draw a similar diagram to represent the mechanical response of the saccule during pitch head tilts. During these head motions, the eyes would elevate and depress to maintain the earth horizon stable. In reality, electrophysiologic and theoretical studies (Pellionisz and Graf, 1987; and Pellionisz and Peterson, 1988) suggest that otolith, ocular and postural responses are not restricted to the pitch and roll head planes but occur in three dimensions as expected.

During horizontal angular head movements, while the horizontal semicircular canals are stimulated, neither the utricle nor the saccule is reoriented relative to gravity. During vertical angular head movements, however, both semicircular canals and otolith organs are stimulated since the semicircular canals are stimulated by the angular head motion and the otolith organs are reoriented relative to gravity. Under these conditions, one could imagine that the otolith organs and the semicircular canals would work synergistically; the semicircular canals signaling the magnitude and direction of the angular head motion, and the otoliths

signaling the axis about which head motion takes place.

The mechanics of both the semicircular canals and the otolith organs have been mathematically modeled (Steinhausen, 1933; and de Vries, 1950) using a second order differential equation that describes the action of a physical system consisting of a mass, a dash pot, and a spring. It has been demonstrated experimentally (Correia et al, 1981; and reviewed in Goldberg and Fernandez, 1984) by recording from vestibular primary afferents that these models, with certain quantitative exceptions, are generally adequate to describe the frequency response properties of the semicircular canals and otolith organs. The predictions of these models generally support the idea that the semicircular canals and otolith organs operate as band-pass filters with the "nonattenuated" part of the response covering the range of frequencies that comprise natural angular head motions and head tilts (Fernandez and Goldberg, 1971; and Fernandez and Goldberg, 1976). This range varies from one species to another, but in humans it ranges from 0.5 to 10 Hz (Guedry and Correia, 1978).

### **Hair Cell Transduction**

There are two types of hair cells found in the vestibular neuroepithelium of the semicircular canals and otolith organs. The long, cylindrical type has been designated as type II, whereas the chalice-shaped hair cell has been designated as type I. Arising from the apical surface of either type of hair cell and embedded in a structure composed of smooth endoplasmic reticulum, ie, the cuticular plate, is the kinocilium and a staircase-arranged group of stereocilia. Near the base and top of the stereocilia are small microfilaments that have been called "strings". Also shown in the cartoon of these generic hair cells are ion channels located on the basolateral surfaces of the hair cell. An unmyelinated nerve calyx surrounds the chalice-shaped type I hair cell or cells, while type II hair cells are innervated by boutons that, through transmission electron microscopy, appear highly vesiculated or slightly vesiculated. It is thought that the vesiculated boutons represent the termination of efferent vestibular nerve fibers onto the hair cells, whereas the calyces and boutons without such a density of vesicles are afferent vestibular terminals. These terminals and their processes are unmyelinated within the vestibular neuroepithelium and typically become myelinated as they exit the basement membrane of the cristae or maculae. It is at this point of myelination that graded postsynaptic potentials that occur on the unmyelinated processes within the neuroepithelium may summate either temporarily or spatially, or both, to produce action potentials seen on vestibular primary afferents.

One current hypothesis for mechano-electrical transduction incorporates a "string hypothesis" (Hudspeth, 1983). This hypothesis suggests that when the stereocilia bend toward the kinocilium, filamentous strings, which connect these cilia, deform and in some way gate ionic channels to open, thereby producing ionic currents within the apical part of the hair cell.

Potassium ions, which are plentiful in the endolymph, flow through the channels, and the resting membrane potential of the hair cell becomes more positive (the cell is depolarized). This depolarization causes voltage-dependent channels in the base of the hair cells that are calcium selective to open. Calcium ions enter the hair cell and trigger another process - exocytosis of synaptic vesicles containing a neurotransmitter. That is, the synaptic vesicles fuse with the outer membrane of the hair cell and release transmitter into the synaptic cleft between the hair cell and the afferent. As the stereocilia return to the pre-deflected,

neutral position, outward potassium currents in the base of the cell cause the cell to repolarize (hyperpolarize) and return the membrane to its resting potential. Deflection of the stereocilia away from the kinocilium has an opposite effect. Since almost all vestibular primary afferents are spontaneously active, it is presumed that some calcium channels are always open and some neurotransmitter is constantly being released. The putative candidates for neurotransmitters at the afferent synapse are excitatory amino acids (Annoni et al, 1984; and Guth et al, 1988). Efferent boutons can be found synapsing on type II hair cells and on the calyces surrounding type I hair cells. Acetylcholine has been implicated as the neurotransmitter for this synapse (Rossi et al, 1980). The mechanisms of action of the efferent vestibular synapse on the hair cells and afferent terminals has not been confirmed but there is evidence (Goldberg and Fernandez, 1980) that, in primates, electrical stimulation of the efferent system has an excitatory effect on the afferent neural activity.

Recent studies (Hudspeth, 1982; and Ohmori, 1985) of enzymatically dissociated solitary hair cells have indicated that aminoglycosides, including streptomycin sulfate and neomycin, act directly to reduce mechano-electric transduction currents in vestibular hair cells.

### **The Neural Processes Within the Vestibular Neuroepithelium**

Although it appears that a single hair cell is innervated by a single afferent terminal, this is not true. The ratio of hair cells to myelinated nerve fibers has been tabulated elsewhere (Correia and Guedry, 1978) and is about 3:1 for the semicircular canals and 5:1 to 6:1 for the otoliths. Figure is a two-dimensional drawing of the branching of unmyelinated afferents and efferents (stippled) in the vestibular neuroepithelium. The drawing summarizes results obtained using transmission electron microscopy and intra-axonal dye tracers such as Lucifer yellow and horseradish peroxidase (Ades and Engstrom, 1965; Correia et al, 1985; Fernandez et al, 1988; and Ross, 1985) that demonstrate several types of innervation patterns on vestibular hair cells. There appear to be three types of specialized afferent terminals. First, as indicated in the figure for the central regions of the vestibular receptors, an unmyelinated calyx may surround part of a type I hair cell (half calyx, HC), one type I hair cell (single calyx, SC), or 2 to 12 type I hair cells (multicalyx, MC). Some calyx terminals, while surrounding a type I hair cell, may branch to form another calyx or may terminate in lightly vesiculated boutons that innervate type II hair cells. This type of terminal may also form a synapse directly on an adjacent type II hair cell. This second type of dimorphic (calyx/bouton) afferent terminal is labeled D in the figure. Finally, in the peripheral regions of the receptor, an afferent fiber may branch to innervate one or more type II hair cells with lightly vesiculated bouton terminals. For any given afferent, each of the types of branching innervation patterns appears to be limited to a region of 50 to 100 microns. Highly vesiculated boutons, thought to be efferent terminals, form *en passant* synapses on type II hair cells and the calyces of type I hair cells.

The categorical architecture of innervation patterns in the vestibular neuroepithelium would appear to be more than coincidental, but the neurophysiology of hair cell innervation has just begun to be studied. It is not clear, for example, whether the graded potentials on the branches of the three types of unmyelinated afferents are different. Nor is it certain that branching over a small distance in the neuroepithelium significantly modifies the cable properties of the unmyelinated afferents. There is, however, evidence (Baird et al, 1988; Honrubia et al, 1981; and O'Leary et al, 1976) that afferents with different types of branching

patterns and those innervating different regions of the cristae and maculae differ in their regularity of action potential firing rate, sensitivity to rotation, and frequency response.

### **Vestibular Primary Afferents and Efferents**

The 18,000 vestibular primary afferent fibers transmit coded sensory information about angular head velocity and head tilts. The average resting discharge (in the primate) is about 90 impulses/sec. Some vestibular afferent fibers fire spontaneously with a very regular discharge, whereas other fibers have a more irregular firing pattern. There is a continuum of regularity of firing patterns. Regularity of discharge appears to correlate with the afferent's firing rate, its frequency response (gain and phase characteristics), and the sensitivity of the afferent (Goldberg and Fernandez, 1984). There is also evidence (Lisberger and Pavelko, 1986) to suggest that afferents with different patterns of regularity of discharge, and hence different response dynamics, project to different central nervous system structures.

The ratio of myelinated afferent fibers to myelinated efferent fibers is about 45:1. The physiologic role of the efferents is still not clear. In monkeys, electrical stimulation of vestibular efferent cell bodies in the brain stem increases the firing frequency of action potentials on vestibular primary afferents (Goldberg and Fernandez, 1980). The bipolar cells for vestibular primary afferents form a superior and inferior ganglion in the internal auditory meatus. The superior and inferior ganglia are formed by the superior and inferior vestibular nerves. The bipolar ganglion cells are generally myelinated and, therefore, probably do not form synapses with each other or another neural process. There is, however, evidence (Kitamura and Kimura, 1983) that some of the ganglion cells are unmyelinated. Generally it seems that the myelinated vestibular ganglion cells serve as bipolar cell bodies for preganglionic processes that innervate the neuroepithelium of the vestibular apparatus and postganglionic processes that terminate within the vestibular nuclei and the cerebellum. Specific pathways associated with projections from each of the vestibular end organs to effector muscles are complicated, have been reviewed elsewhere (Correia and Guedry, 1978; and Goldberg and Fernandez, 1984), and are beyond the scope of this chapter.