A place principle for vertigo

Richard R. Gacek *

Department of Otolaryngology, Head and Neck Surgery, University of Massachusetts Medical School, Worcester, MA 01655, USA

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Abstract

Objective: To provide a road map of the vestibular labyrinth and its innervation leading to a place principle for different forms of vertigo.

Method: The literature describing the anatomy and physiology of the vestibular system was reviewed.

Results: Different forms of vertigo may be determined by the type of sense organ, type of ganglion cell and location in the vestibular nerve.

Conclusion: Partial lesions (viral) of the vestibular ganglion are manifested as various forms of vertigo.

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Keywords: Vertigo; Vestibular nerve; Pathology

Contents

1. Introduction .............................................................................. 1
2. Sense organ ............................................................................... 2
3. Ganglion cells ............................................................................. 4
4. Hair cells .................................................................................. 5
5. Hair cell polarization ................................................................. 5
6. Efferent vestibular system ............................................................. 8
7. A place principle for vertigo ...................................................... 9
8. Conclusion .............................................................................. 10
References ................................................................................. 10

1. Introduction

Sensory systems must be highly organized to function effectively. The special senses are especially well developed. This organization exists at the periphery and is duplicated with ascent of the system centrally. The auditory system provides an excellent example of a place principle for hearing. The reception of frequencies in orderly fashion from low at the apex of the cochlea to high at the base is determined by the physical characteristics of the cochlear partition. Components in the cochlear duct (basilar membrane, spiral ligament, support cells in the organ of Corti) determine the place for maximal displacement of this partition by a given traveling wave induced by an auditory stimulus. This orderly transmission of frequencies is preserved over the primary auditory neuron, and multiple central neurons to the cortex for proper integration of auditory messages. Vision and olfaction have a similar precise organization to their neural systems.

Sufficient morphologic, physiologic and clinical evidence has accumulated in the past few decades to indicate an organization in the vestibular system that may account for different forms of vertigo depending on the location of pathology in the vestibular nerve. The evidence supporting such a “place principle for vertigo” will be reviewed in this...
Such a principle might aid our clinical approach to the evaluation and treatment of vertigo in patients, with recurrent vertigo. The recurrent vestibulopathies are now known to be caused by discrete vestibular ganglion cell lesions, likely viral induced. A significant body of histopathologic evidence has demonstrated that viral lesions are limited to discrete clusters of degenerating neurons in the vestibular ganglion in vestibular neuronitis, Meniere’s disease and benign paroxysmal positional vertigo (Fig. 1) [1–3]. This pattern of ganglion cell loss is typical of a viral neuropathy (4) caused by re-activation of a latent neurotropic virus (e.g. Zoster) [4]. Because the description of dizziness by patients may vary (i.e. vertigo, unsteadiness, positional vertigo), attempts have been made to classify vestibular disorders according to the nature of the imbalance symptom. An example of such a knowledge based system is that of Mira et al. [5]. This system used vertigo and dizziness to divide a long list of clinical pathologies encountered by the otologist or neurologist.

The organization of the peripheral vestibular system is determined largely by two anatomical features. These are: (1) type of sense organ. (2) Type of ganglion cell.

2. Sense organ

Of the two types of vestibular sense organs, the otolith organs are probably the most important in a gravity dependent environment. They are the oldest phylogenetically with the canal system making a presence as more mobility (swimming, walking, running) was acquired. Since the otolith organs feature a covering membrane containing high specific gravity (2.71) calcium carbonate particles (otoconia) resting on the ciliary bundles of the hair cells in the sensory epithelium, they are in a constant state of stimulation (Fig. 2). The canal system, on the other hand, is activated by transitory increases in angular acceleration or deceleration of the fluid (endolymph) within the membranous canal. Such inertial changes deform the cupular partition of the ampullary enlargement in the canal resulting in deflection of the ciliary bundles of hair cells in the sensory epithelium (Fig. 3) [6].
The otolith organs are arranged horizontally (utricle macula) and vertically (saccule macula) to record position and position change in these two planes. There is some anatomical evidence which suggests each macula actually represents the merging of two smaller maculae with oppositely polarized hair cells (Fig. 4). The interface of this merging is located at the striola line. The vestibular nerve and ganglion supplying afferent innervation to the vestibular sense organs has an arbitrary division into superior and inferior. The superior division supplies the utricular macula, the crista of the lateral and superior semicircular canals and a small portion of the saccular macula while the inferior division innervates the saccule and posterior canal crista (Fig. 5).

The bipolar vestibular ganglion cells which supply afferent input from the otolith organs are located ventrally in the central portion of the ganglion (Fig. 5), while the canal ganglion cells are located at the rostral and caudal ends [7]. As the axons from these ganglion cells form the vestibular nerve trunk, those from the canals converge together in the rostral half of the nerve trunk and the otolith axons in the caudal half. This differential location of otolith and canal neural input is necessary because of their different connections with second order neurons in the vestibular nuclei. The canal projections bifurcate on entering the brainstem with the ascending branch terminating in the superior vestibular nucleus (SVN) and the descending branch ending in the medial vestibular nucleus (MVN) (rostral part) (Fig. 6). These two nuclei project bilaterally into the medial longitudinal fasciculus (MLF). The SVN projects in the ipsilateral MLF to the IV and III nerve nuclei while the MVN sends a comparable projection in the contralateral MLF to terminate in the IV and III nuclei in a reciprocal fashion [8]. These pathways serve the vestibulo-ocular reflex (VOR) for vertical and oblique extraocular movements necessary for nystagmus. The MVN also projects bilaterally to the VI nerve nucleus and to the ipsilateral medial rectus subnucleus in III n. over a tract called the ascending tract of Deiters. These projections are responsible for the horizontal VOR. Some projections from
the medial and descending vestibular (DVN) nuclei travel down the MLF to the muscles of the neck region where they are responsible for vestibulo-collic reflexes [8,9].

The bifurcating axons from the otolith organs terminate in the caudal vestibular nuclei—that is the lateral (LVN), medial and descending nuclei (Fig. 7). The ascending branches from utricular neurons terminate in the ventral portion of the LVN and in the rostral MVN [7]. The descending branches connect with cells in the caudal MVN and DVN. The LVN is responsible for vestibulospinal tract activation of trunkal and limb muscle reflexes [9,10]. The MVN and DVN descend in the MLF for cervical muscle reflexes. However, the utricle also has connections with the VI and III nuclei for horizontal eye movements (compensatory).

Input from the saccule is similar but much smaller. Saccular neurons project to portions of the MVN and DVN for neck muscle activation via the MLF. Projections to the oculomotor nucleus over the group Y nucleus permit a VOR response from the saccule involving the superior and inferior rectus muscles as well as the oblique eye muscles (Fig. 8) [11].

In summary, the semicircular canal sense organs primarily project to the nuclei for VOR activation (nystagmus) while the otolith organs are responsible for activity in anti-gravity muscles of the neck, trunk and limbs (ataxia). However, compensatory eye muscle activation also occurs from stimulation of the otolith organ pathway.

3. Ganglion cells

Since the inner ear and its sense organs with their nerve supply, develops from the same anlagen, it is not surprising that two types of ganglion cells, as described in the spiral ganglion of the cochlea, also exist in the vestibular nerve. The two types of ganglion cells in these two types of sense organs have similar features in morphology, physiology and pathologic behavior.

Type I ganglion cells have large caliber myelinated appendages (dendrites) which innervate type I hair cells with 1:1 or almost 1:1 ratio (Fig. 9). They possess an irregular spontaneous discharge pattern and degenerate following ablation of the sense organ (Fig. 10) [12–14]. In the cochlea they provide 90% of the innervation of the organ of Corti where they supply inner hair cells (IHC) [15]. Type I ganglion cells are sequestered from the type II cells in the vestibular ganglion forming the ampullary nerves but have a dispersed pattern in the nerves to otolith organs [7]. This distribution reflects their periphery termination on type I HC. The dendrites of type I ganglion cells travel in the center of ampullary nerves because they terminate on the type I hair
cells which are concentrated at the crest of the crista ampullaris [16,17]. These hair cells are positioned to be most sensitive to cupular displacement.

The central projection of type I ganglion cells is to vestibulo-ocular neurons in the SVN and MVN via axosomatic synapses (Fig. 11) [18]. Thus the type I hair cell – type I ganglion cell – vestibulo-ocular neuron in the vestibular nuclei (SVN, MVN) is responsible for the VOR responses associated with stimulation or degeneration of the cristae ampullaris. In the otolith system these type I ganglion cells project to large multipolar neurons of the vestibulospinal tracts as well as to vestibulo-ocular neurons in the caudal vestibular nuclei.

Type II ganglion cells have small caliber myelinated dendrites which, innervate type II hair cells in a diffuse manner [16,17] (i.e. many HC supplied by a single fiber) (Fig. 9), and demonstrate a regular spontaneous discharge pattern [12,13,19]. They do not degenerate after end organ ablation (Fig. 10) [18]. The type II hair cells located along the slopes of the crista ampullaris are not in a position to optimally respond to cupular displacement but may have a supporting role in end organ sensitivity by virtue of their rich efferent innervation.

Because the lateral canal sense organ is a recent phylogenetic development, making an appearance in amphibians (frog), the type I and II ganglion cell populations are separated in the superior division ganglion [7,20]. The type I ganglion cells are concentrated at the most rostral end of the ganglion while type II cells occupy the caudal region of the superior division ganglion (Fig. 5). The dendrites of type II ganglion cells envelop those of type I ganglion cells as the ampullary nerves are formed. This separate location of type I and II ganglion cells in the superior vestibular division has been confirmed in the monkey and human vestibular nerve [20] and provides an opportunity for a differential functional response from injury to either of these two types of neurons.

4. Hair cells

The two types of hair cells (HC) in the vestibular organs are somewhat similar to the inner (HC) and outer hair (OHC) cells in the organ of corti. The type I HC in the vestibular organs (i.e. crista) are innervated by type I vestibular ganglion cells with the same irregular spontaneous electrical activity as the type I spiral ganglion cells which innervate the IHC in the organ of corti [15,16]. In both systems they are responsible for the major afferent input to the brain for balance and hearing.

The type II vestibular hair cells may play an enhancing role in the sensitivity of balance organs similar to the role that OHC impose on the IHC and auditory sensitivity. The contractile properties of OHC allow a change in the cochlear amplifier effect in the organ of corti [21]. This contractile function of the OHC is under efferent neural control and serves to enhance the sensitivity of auditory neurons (type I).

5. Hair cell polarization

In addition to the different functionalities of two types of HC (with their innervation) in the vestibular system, an important feature of vestibular hair cells is their alignment within an individual sense organ and the relationship of this orientation to that of other sense organs in the labyrinth [16,17]. This is referred to as the “polarization of hair cells” in the labyrinth.

In contrast to cochlear hair cells vestibular HC have a ciliary bundle comprised of 70–100+ stereocilia and one longer Kinocilium [16,17]. This Kinocilium is located at the end of the ciliary bundle where the longest stereocilia are located. The significance of this arrangement is that when the cilia are deflected toward the kinocilium there is depolarization of the HC and an increase in the afferent neural unit activity while deflection away from the kinocilium results in hyper-polarization and a decrease in neural activity [16]. This has great functional significance and accounts for the different responses obtained by testing individual canals by warm and cool caloric stimulation.

An equally important consideration, however, is the relationship of this polarity of HC between the five sense organs of the labyrinth. Any movement of the body and head...
produces activation or deactivation in all sense organs of both labyrinths. Figs. 12 and 13 summarize this polarity of HC in the sense organs or parts of sense organs (maculae) [16,17]. It is obvious that the polarization of HC in coplanar canals is opposite to each other. In this way, a given rotation produces excitation in one canal and decreased neural input from the opposite coplanar canal, greatly enhancing the differential response delivered to the brainstem for a VOR response. This difference in the input is also enhanced by commissural inhibition of the contralateral canal by activity generated by the activated canal.

The relationship between the canals and otolith organs is important but under recognized. Experiments conducted in both zero gravity and one gravity environments have demonstrated a modulation of canal responses by stimulation of the otolith organs [22–24]. Fluur and Siegborn have shown this in the cat [25]. They demonstrated that selective denervation of an otolith (the utricle) produced a horizontal nystagmus if the innervation to the lateral canal crista was intact. However, if the lateral canal sense organ was denervated before selective denervation of the utricle, no nystagmus was observed. A similar relationship between the saccule and the posterior canal was observed. These observations indicate that there is an inhibitory effect on canal responsiveness by the otolith of the same vestibular nerve division.

Normally a change in head position produces a force that causes excitation of the otolith and its corresponding canal. However, if the otolith function is deficient, its corresponding canal will respond in an excitatory mode [22]. This could be reflected in a position provoked vertigo and nystagmus. It has been suggested that this otolith–canal relationship is based on a velocity storage mechanism in the central nervous system probably the vestibular nuclei [26]. The polarization of HC in the otolith and corresponding canal sense organs play a role in this relationship. As seen in Figs. 12 and 13 the maculae are each divided into halves by the striola line with each half containing oppositely polarized HC. Each half has HC that are aligned with a crista ampullaris. These would be activated by the same vector during movement of the head.

The number of neural units supplying the otolith and canal sense organs is important in understanding the vulnerability of this otolith–canal interrelationship. In the mammalian ear where numerical data are available for the innervation of individual vestibular sense organs (guinea pig, cat, monkey), the number of afferent neural units in the vestibular nerve branches is approximately equal [27]. However, the otolith innervation modulating each crista ampullaris is represented by one half the total innervation of the macula, making the effective otolith neural input one-half that supplying the crista ampullaris. Quantitative assessment of the vestibular ganglion

Fig. 9. Diagram of the innervation to the two types of vestibular hair cells.
of TB from patients with BPPV have shown a greater than 50% loss of ganglion cells in both vestibular divisions [28]. A loss of this magnitude in afferent units already a fraction of those to the crista ampullaris is likely to cause a disruption in the otolith-canal relationship resulting in BPPV.

This neuropathologic explanation may account for the various categories of BPPV. Posterior canal BPPV is by far the most common possibly because the saccular nerve is the smallest in all species studied [27]. Thus it represents the greatest mismatch between otolith and canal innervation and most likely to lose its inhibitory effect on posterior canal
excitation. Lateral canal and anterior canal BPPV are less commonly recognized because of a smaller mismatch between otolith and canal innervation.

6. Efferent vestibular system

The final form of vestibular injury which may present as dysequilibrium relates to the efferent vestibular pathway. The vestibular efferent pathway originates bilaterally in the MVN just lateral to the abducens nucleus [29]. Axons of these neurons [30] merge with and travel with the efferent cochlear pathway (olivo-cochlear pathway) in the vestibular nerve as it exits the brainstem (Fig. 14) [31]. This common efferent bundle is clearly demonstrated by the high acetetyl cholinesterase activity which suggests acetylcholine as its neurotransmitter agent (Fig. 15) [32]. This efferent bundle passes through the saccular portion of the vestibular ganglion and, therefore, may be affected (loss of function) by inflammatory lesions in this area (Fig. 16). Individual efferent axons ramify as they travel in a dispersed arrangement to the sense organs (Fig. 17). This branching pattern permits a rich efferent termination on HC in the sense organ neuroepithelium.

Although an inhibitory effect is associated with stimulation of the vestibular efferent pathway [33–35], the function of this neural system in balance has not been demonstrated. However, certain established facts on efferent systems permit speculation on the role that the efferent system may play in balance.

The role of the efferent cochlear pathway has been shown to be one of modifying the physical characteristics of the sense organ to enhance sensitivity for stimulation of the primary auditory unit. By activating the contractile potential of the OHC to lengthen or shorten thus adjusting the reticular lamina and the tectorial membrane to sharpen the tuning curves for the primary auditory units (IHC and type I spiral ganglion cells) [21]. Otoacoustic emissions (OAE) generated by this "cochlear amplifier" [36] have been shown to be

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**Fig. 14.** Diagram of the efferent vestibular pathway (solid lines); stippled area = efferent cochlear pathway. LVN: lateral vestibular nucleus; MVN: medial vestibular nucleus; DCN: dorsal ventral cochlear nuclei; VCN: ventral cochlear nuclei; VII: genu of facial nerve; VI: abducens nucleus; ASO: accessory superior olivary nucleus; LSO: lateral superior olivary nucleus.

**Fig. 15.** Transverse section of the vestibular (V) and cochlear (C) nerves in the cat shows the efferent labyrinthine pathway (arrow) in the center of the vestibular nerve. Acetylcholinesterase preparation. F: facial nerve.
inhibited by the activity of the crossed (efferent) olivocochlear pathway.

Efferent vestibular activity in lower forms (fish) has been shown to be increased before vigorous movement (swimming) which would over stimulate the organ of balance (lateral line) [37–39]. Presumably this efferent activation is intended to reduce (prevent) self-stimulation by the animals activity. This a role is compatible with the numerous demonstrations of inhibition of afferent neural transmission following stimulation of the vestibular efferent system [33,34]. Such a system may play a role in preventing auto stimulation of vestibular sense organs during physical activity.

A suggested corollary in the vestibular system would be for the efferent pathway to prevent auto-stimulation of sense organs by mechanically changing the sensitivity of the sense organs by altering the covering membrane (cupula, otoconial blanket) during vigorous physical activity. The clinical syndrome that could result from dysfunction of the efferent vestibular system might be motion sickness. A particularly efficient efferent system would be a requirement for a gymnast or figure skater.

7. A place principle for vertigo

This anatomical organization (supported by physiological correlates) provides a basis for attributing various forms of vertigo to pathology in discrete part of the vestibular ganglion. There is increasing pathologic evidence that the recurrent vestibulopathies (ventricular neuronitis, Meniere’s disease, benign paroxysmal positional vertigo) are caused by discrete ganglion injury (degeneration) from reactivation of neurotropic viruses (herpes virinae family) [1–3]. The severity and form of dysequilibrium described by such patients will depend on the location and number of vestibular ganglion cells injured by virus [40]. The location of sites in the vestibular ganglion responsible for different forms of vertigo are represented by the numbers 1–5 in Fig. 5.

1. Lesions in the most rostral part of the vestibular ganglion (type I GC) are responsible for episodes of rotatory vertigo. A strong VOR disturbance (nystagmus) signals this form of vertigo.

2. If the ganglion cell lesion is located immediately caudal to this rostral pole of the superior division type II GC are affected. Unsteadiness, especially on head movement, will be experienced because these type II GC project to commissural pathways.

3. Degeneration of ganglion cells in ventral parts of both the superior (utricle) and inferior (saccule) divisions of the vestibular ganglion, causes loss of function in the vestibulospinal tract to neck, trunk and limb muscles. Frequently these are described by patients as “drop” attacks. Ataxia may be a lingering form of this form of dysequilibrium.

4. The most common form of vertigo encountered in practice is position induced. Short duration episodes of a rotatory vertigo which is fatiguable have been described since Barany [41]. Both Barany [41] and Citron and Hallpike [42] felt this was an otolith disorder but the nystagmus response observed in this syndrome prevented acceptance of an otolith cause. Hallpike’s description of utricular degeneration [42] in the TB of BPPV was not enough to neutralize the predominant support of a canal etiology. Although the clinical response is a rotatory form of vertigo, the uninhibited response is caused by loss of the inhibitory role of the otolith organs.

5. Lesions in the saccular portion of the vestibular ganglion (inferior vestibular) may secondarily interrupt the efferent pathways to the cochlear and vestibular sense
organs. Clinically, the loss of this control may be perceived as tinnitus and motion sickness.

8. Conclusion

This review is an attempt to provide a guide to pathologies involving portions of the peripheral vestibular pathway. It is unusual that only a specific location of pathology will be present in a given patient. More often, a mixture of locations will be present. However, the goal here is to establish a map or framework to guide the evaluation and management of patients with recurrent vestibulopathy.

References