Published in final edited form as:
Audiol Med. 2009 December 1; 7(4): 180–188.

Advances in Auditory and Vestibular Medicine

Mohamed A. Hamid, MD,PhD,EE,
Professor of Audiology and Otolaryngology, Founder and Medical Director, The Cleveland Hearing and Balance Center, 29001 Cedar Rd, #203, Lyndhurst, Oh, 44124, USA, 01(216) 684-9970, hamidma@ClevelandHearingBalance.com

Dennis R. Trune, Ph.D., MBA, and
Oregon Hearing Research Center, Department of Otolaryngology/Head and Neck Surgery, Oregon Health & Science University, Portland, OR 97239

Mayank B. Dutia, PhD
Centre for Intergrative Physiology, University of Edinburgh, Hugh Robson Building, George Square, Edinburgh EH8 9XD, UK

Abstract

Auditory and Vestibular medicine is becoming more accepted as a specialty of its own, Medical NeurOtology. Recent advances in the field have been instrumental in the understanding of the scientific foundations, pathophysiology, clinical approach and management of patients with hearing and vestibular disorders. This paper will review these advances.

Keywords

Auditory and Vestibular Medicine; Ion homeostasis of the inner ear; vestibular compensation; vertigo; hearing loss; Meniere's disease; vestibular migraine; BPPV; intratympanic perfusion; vestibular rehabilitation

Introduction

Auditory and vestibular medicine, also known as Medical NeurOtology, is an evolving medical specialty that focuses on disorders and diseases of the inner ear and related central nervous system structures. Auditory and vestibular medicine physicians should be well versed in general medicine, neurology and otology. Additional knowledge in neuroscience, physics, engineering and acoustics is also important. At the moment, the specialty is well positioned in Europe as compared to other parts of the world. Hearing loss is the most common handicap in the world. In the industrialized world, the incidence of hearing loss is 25% in people under age 25 and reaches 40% in persons over age 40. Congenital and prelingual deafness occurs in 1/1000 children. Tinnitus is reported by 25% of the population. The incidence of dizziness, vertigo and/or imbalance is 5-10% and reaches 40% after age 40. The incidence of falling is 25% in subjects over 65. Falling can be a direct consequence of vestibular diseases, especially in patients with multiple sensory deficits. Migraine is a more prevalent disorder (10%) than Meniere's disease (< 1%). However, vertigo and motion sickness are present in 30% and 50% respectively of migraine patients, which makes it difficult sometimes to distinguish migraine-associated dizziness from primary inner ear diseases.

Correspondence to: Mohamed A. Hamid.

Advances in the understanding of inner ear molecular biology, genetics, regenerative medicine, ion homeostasis, electrophysiology and diagnostic modalities have increased our abilities to further understand inner ear disease and develop new management strategies. Central to these advances is the departure from viewing the inner ear as a fluid based system to the more physiologically based view as an ionic transport system. Also critical are the continual advances in understanding the processes underlying auditory and vestibular rehabilitation and compensation following diseases affecting these systems.

The work up of patients with inner ear disorders and diseases requires time and resources that are gradually diminishing given the current medical economics worldwide. Consequently, the demand on Auditory and Vestibular physicians to manage these patients in a cost effective manner has increased over the last decade. This review will discuss recent advances in the field with emphasis on recent basic science findings and their potential clinical applications.

Ion Homeostasis in the Ear

The inner ear is essentially an organ of ion homeostasis and can function properly only if its ion balances are tightly controlled. Any disruption of normal ion transport will significantly compromise hearing and balance. These ion-regulated functions include endolymph and perilymph production, hair cell transduction, and nerve conduction. There are dozens of ion transport channels and transporters in the inner ear, and undoubtedly more will be characterized[1]. The majority move K^+, Na^+, Ca^{++}, Cl^-, H^+, ^-OH, HCO_3^-, as well as other ions[2–4]. However, there are other factors that control fluid and ion movements, including atrial natriuretic peptides, aquaporins, and transient receptor potential vallinoid ion channels[5–8]. Inner ear ion transporters and channels are controlled by numerous natural hormones, such as aldosterone (mineralocorticoid), cortisol or hydrocortisone (glucocorticoid), diuretics and anti-diuretics (vasopressin), thyroid hormone, and estrogen, as well as nucleotides and other enzymes[9–12]. Thus, abnormal levels of these hormones can impact inner ear physiology. Also, many of these ion transport channels and transporters are absent or defective in various genetic disorders, making an understanding of their functions critical for the evaluation of congenital hearing disorders[4;13–15].

Perhaps the best studied ion homeostatic mechanism is that of K^+ transport, which is tied closely to that of Na^+. Endolymph requires a higher K^+ content than perilymph (high Na^+) to maintain the endocochlear potential and allow hair cell depolarization. Therefore, many transporters and channels are in place to keep K^+ moving into the endolymph, through the hair cell into the perilymph during transduction, and cycling back to the endolymph. Because the composition of endolymph is similar to intracellular fluid, a hair cell could not function if it was surrounded by endolymph (no potential difference). This dilemma is solved by surrounding the stereocilia with endolymph to provide the necessary high K^+, but surrounding the cell body (beneath the reticular lamina) with perilymph, which is similar to extracellular fluid. Once K^+ exits the hair cell and enters the extracellular (perilymph) space, a series of gap junctions (connexins) move K^+ through the supporting cells to the spiral ligament fibrocytes, and up to the stria vascularis for its transport back into the endolymph. There also appear to be other medial or lateral routes taken by K^+ to eventually reach the stria[16;17]. Once K^+ reaches the stria vascularis, it is moved into the endolymph through a series of transporters and channels, including several K^+ channels, Na^+,K^+-ATPase, Na^+-K^+-$2Cl^-$, and possibly others. Most of these K^+ transport mechanisms are under the control of the mineralocorticoid aldosterone and the antidiuretic vasopressin.

There are a number of disorders that compromise this movement of K^+ and cause hearing loss. Congenital genetic defects occur in the gap junction connexins, the various K^+

channels, or other ion channels that are need to work in tandem with the K^+ channels[4;18–22]. Furthermore, disruption of the endothelial cell tight junctions in the stria due to connexin defects also can lead to hearing loss by eliminating the endocochlear potential[23;24]. It has been demonstrated that stria intermediate cells, basal cells and fibrocytes are all interconnected by gap junctions, with the syncitium possibly including endothelial cells, as well[24;25]. Thus, K^+ cycling and transport can be compromised by gene defects or disease processes that affect any of these cellular components. It also has been reported that loss of aldosterone with aging may lead to presbycusis, possibly by interfering with this process[26]. The impact of glucocorticoids on this mineralocorticoid function also has been shown experimentally[27–29] suggesting the K^+ transport system may respond to therapeutic anti-inflammatory steroids, such as prednisone and dexamethasone.

Vestibular functions also are rigidly tied to inner ear ion homeostasis and the same ion channels described above appear throughout the vestibular sensory epithelia. The dark cells surrounding these epithelia, and their adjoining duct cells, house numerous ion channels that maintain similar ion homeostatic processes[2;30–32]. Like in the cochlea, ongoing studies are beginning to clarify these channels and what natural or therapeutic steroids control their functions.

Vestibular Compensation

'Vestibular compensation' (VC) is a general term for the behavioral recovery of oculomotor and postural control that occurs after damage to the vestibular system. In its most widely-studied form, VC refers to the recovery after a permanent loss or deafferentation of the semicircular canal and macular receptors of one inner ear (e.g. after unilateral labyrinthectomy, or vestibular neurectomy). Because the vestibular loss is permanent, it is accepted that VC must involve extensive synaptic and neuronal plasticity in the brainstem vestibular nuclei, cerebellum, and related brain areas[33–35]. Similar forms of VC, no doubt with common brain plasticity mechanisms, also take place after the partial or incomplete loss of peripheral vestibular inputs. In the clinical context peripheral vestibular damage may often occur gradually over a prolonged time, in which case VC is also an ongoing process which continuously attempts to normalize oculomotor and postural motor control.

Mechanisms of vestibular compensation

Experimental studies have shown that unilateral vestibular deafferentation (UVD) has profound effects on the activity of vestibular nucleus (VN) neurons. Of the four main vestibular nuclei in the brainstem, the most extensively studied is the medial vestibular nucleus (MVN). Immediately after UVD the normally high resting discharge of the majority of MVN neurons on the ipsi-lesional side is virtually abolished, while the activity of contra-lesional MVN neurons is either normal or increased. The silencing of ipsi-lesional MVN neurons is due not only to the loss of primary afferent excitation from the lesioned labyrinth, but also to an increased commissural inhibition from the contra-lesional side. The subsequent amelioration of the initially severe symptoms (ocular nystagmus, head and body roll and yaw tilt, postural instability) is broadly correlated with a recovery of resting activity in ipsi-lesional MVN neurons to near-normal levels, and a "re-balancing" of the commissural inhibitory system. Much research has therefore focused on understanding the causes of the initial silencing of the ipsi-lesional MVN cells after UVD, and the mechanisms that may bring about the recovery of their resting activity early in VC.

On the basis of experimental evidence, at least four candidate synergistic mechanisms have been proposed which may be important in the early stages of VC[34].

1. *Changes in the responsiveness of vestibular nucleus neurons to inhibitory neurotransmitters GABA and glycine.* Studies of *in vitro* slice preparations of the brainstem have revealed many of the electrophysiological characteristics of MVN neurons and the actions of various neurotransmitters that influence vestibular function. Comparison of the responsiveness of MVN neurons to the inhibitory neurotransmitters GABA and glycine, in slices from normal animals and animals that had compensated for various times after UVD, showed that the sensitivity of the ipsi-lesional MVN neurons to these inhibitory transmitters is significantly down-regulated. This is appropriate to counteract the enhanced commissural inhibition to which the ipsi-lesional MVN cells are subjected after UVD, and so may help to restore their resting discharge early in VC.

2. *Changes in the electrophysiological excitability of vestibular nucleus neurons after deafferentation.* In parallel, ipsi-lesional MVN cells also up-regulate their intrinsic electrophysiological excitability. This involves changes in their input resistance and resting membrane potentials, and a potentiation of their responsiveness to synaptic inputs through the up-regulation of appropriate ion channels. In particular there is an increase in the number of cells that show low-threshold calcium spikes (LTS), which may significantly increase their responsiveness to their remaining non-vestibular synaptic inputs. In the longer term these changes in intrinsic properties of the ipsi-lesional MVN neurons persist, and additional changes also occur in the properties of contra-lesional MVN neurons. The excitability, neurotransmitter sensitivity and signal-processing characteristics of the vestibular neurons are therefore permanently modified over the course of VC.

3. *Adaptive changes in synaptic connectivity in the vestibular reflex networks.* In the course of VC over several weeks, the synaptic connectivity of excitatory and inhibitory pathways in the brainstem vestibular networks also undergoes gradual, activity-dependent re-organisation. Thus MVN neurons that are deprived of their original synaptic inputs after deafferentation, become responsive to excitatory inputs from other, intact afferents. This substitution of inputs through synaptic re-organisation is similar to that in other sensory systems. For example, the area of the somatosensory cortex concerned with a particular body part gradually becomes responsive to inputs from adjacent regions if its normal input is deafferented. In the vestibular nuclei, such ‘re-wiring’ of synaptic connectivity has the benefit that the deafferented MVN neurons receive substitute excitatory inputs which may restore and maintain their activity. However, the re-wired connections may now generate quite inappropriate vestibular reflexes. For example, MVN neurons previously concerned with horizontal canal afferents may now receive synaptic excitation from macular afferents and generate horizontal eye movements in response to vertical head movements. An important part of the overall behavioural recovery in VC may therefore involve the suppression of such inappropriate reflexes, for example by alternative strategies for gaze stabilization.

4. *Post-lesional changes in the control of vestibular nucleus neurons by the cerebellum.* While the cerebellum, and in particular the flocculus, has long been known to be important in calibrating the gaze-stabilizing function of the vestibulo-ocular reflex (VOR), its role in VC has been unclear. Ocular nystagmus in flocculectomised animals eventually disappears completely, suggesting the flocculus is not essential for VC. Other processes, such as those discussed above, also may achieve compensation, but over a longer time period. However for the normal development of VC, and the relatively rapid subsidence of nystagmus within a few days, the flocculus appears to play an important, but as yet unclear, role.

Interactions between stress and brain plasticity during VC

The development of vestibular compensation after UL is significantly affected by stress, as well as conditions such as anxiety and depression, where the normal function of the hypothalamo-pituitary-adrenal (HPA) stress axis is altered[34;36]. Glucocorticoids (GCs) released by the adrenal cortex in response to stress have important modulatory effects on neuronal and synaptic function in the brain. GCs may act directly on membrane ion channels and neurotransmitter receptors, or they may alter gene expression in neurons through specific intracellular receptors (glucocorticoid receptors, GRs or mineralocorticoid receptors, MR); and they may be rapidly converted to active neurosteroids.

A number of studies suggest that glucocorticoids and neurosteroids modulate vestibular system function and compensation[37–41]. Anxiety and stress in patients with vertigo significantly delays the recovery from vestibular symptoms. Conversely, treatment of patients with the methylprednisolone has been reported to improve VC. In animal models both the behavioral recovery and the changes in electrophysiological properties of MVN neurons, are facilitated by dexamethasone and inhibited by the GR antagonist RU38486[42]. However, a critical level of stress activation appears to be required, since additional stress in the form of restraint applied to compensating animals after UVD retards VC. Such interactions may have important implications for patients with balance disorders. Effective vestibular rehabilitation after vestibular loss is achieved by exercise and training which involves stimulation of the visual and somatosensory systems, presumably allowing activity-driven sensory substitution in the central vestibular pathways[43;44;44]. It may also be relevant that such exercises also stimulate a moderate stress response that may facilitate brain plasticity. Slow or incomplete compensation in some patients could involve altered responses to stress, as in depression or anxiety, though this remains to be established.

To what extent can remaining sensory information and/or sensory biofeedback (BF) compensate for loss of vestibular information in controlling postural equilibrium? The primary role of the vestibulospinal system is as a vertical reference for control of the trunk in space, with increasing importance as the surface becomes increasingly unstable. Our studies with patients with bilateral loss of vestibular function show that vision or light touch from a fingertip can substitute as a reference for earth vertical to decrease variability of trunk sway when standing on an unstable surface. However, some patients with bilateral loss compensate better than others, and those with more complete loss of bilateral vestibular function compensate better than those with measurable vestibulo-ocular reflexes. In contrast, patients with unilateral vestibular loss (UVL) who reweight sensory dependence to rely on their remaining unilateral vestibular function show better functional performance than those who do not increase vestibular weighting on an unstable surface. Light touch of <100 grams or auditory biofeedback can be added as a vestibular vertical reference to stabilize trunk sway during stance. Postural ataxia during tandem gait in patients with UVL is also significantly improved with vibrotactile BF to the trunk, beyond improvements due to practice. Vestibular rehabilitation should focus on decreasing hypermetria, decreasing an overdependence on surface somatosensory inputs, increasing use of any remaining vestibular function, substituting or adding alternative sensory feedback related to trunk sway, and practicing challenging balance tasks on unstable surfaces. Irrespective of which format or setting of vestibular rehabilitation, it must stimulate and gradually challenge the vestibulocoular, vestibulospinal and their visual interaction to initiate and maintain VC[44].

Regenerative medicine and the inner ear

The application of regenerative medicine[45] , molecular genetics[46], and the use of embryonic stem cells to create inner ear hair cells has been rapidly advancing since it was shown that

birds have the ability to rebuild damaged auditory hair cells[47]. Several studies are currently exploring different cell lines, genetic vectors and autologous cells to circumvent rejection and to increase survival and functionality of regenerated cells[48–51]. Detailed discussion of this subject is beyond the scope of this review. Suffice to say that it is of critical importance to the future of Auditory and Vestibular Medicine as it will impact the management of most if not all types of hearing and vestibular diseases.

Clinical Approach to patients with Auditory and Vestibular Disorders

In medicine, history and physical examination are the corner stones of optimal medical care. This is particularly true in Auditory and Vestibular Medicine[52]. The history of hearing loss in children should include pregnancy and delivery problems and family history of hearing loss. In adults, history of ototoxic medications, noise exposure, ear disease or surgery, and allergies should be included. Fluctuating hearing, aural fullness or pressure and tinnitus should be documented. In eliciting the history of vertigo, dizziness or imbalance, patients should be guided when necessary to classify “dizziness” into two main categories; vertigo and non-vertigo. This dichotomy is helpful as rotational vertigo is often due to inner ear disease whereas non-vertigo symptoms may be due to CNS, cardiovascular or systemic diseases. Incoordination and inability to walk during episodes can be due to cerebellar diseases, especially in the elderly population. Continuous dizziness, motion sensitivity, drop attacks and falls should be evaluated. History of migraine, head trauma and prior viral illness is important. The history should include careful review of systems and screening for anxiety/depression. History of prescription medicines, over-the-counter medications, herbal medicines and recreational drugs (including smoking and alcohol) is helpful to identify “pharmacologically” induced dizziness/lightheadedness.

Traditional medical, neurological and ENT examination of hearing loss and vertigo are important. The ear exam should be done with a microscope when possible, especially in patients with prior ear surgery or recent ear trauma. Hearing can be screened using tuning forks. Vertigo patients in particular require an additional/complementary “Vestibular Examination” which focuses on neck and eye movements, and vestibular and postural responses. The neck is examined for range of motion, stiffness and provoked symptoms. Eye movements are examined in all cardinal directions in searching for gaze, spontaneous, post head shake and positional nystagmus. Central nystagmus is purely horizontal or vertical and is seen with visual fixation. Peripheral nystagmus is usually rotatory and is present with removing optic fixation (e.g. under closed eyelids, use of Frenzel’s glasses or video monitoring). A fairly reliable clinical impression of the horizontal and vertical vestibular ocular reflex (VOR) can be ascertained by observing (or video taping) the presence, ‘intensity” and symmetry of per-rotatory nystagmus during and after active head movements by the examining physician (or by rotating the patient’s exam chair manually). With time and experience, unilateral and bilateral reduced vestibular responses can be determined during this test. Nystagmus and vertigo symptoms during the Dix-Hallpike exam are typical findings in benign positional vertigo (BPPV). Focused neurological examination of the cranial nerves, motor and sensory modalities, gait and stance are important at the initial visit. Cerebellar tests, especially failure of fixation suppression, are important to check the vestibulo-cerebellum. Failure of fixation suppression can be tested in the office by asking patients to stretch their arms and look at their thumbs while being passively rotated (manual rotation of examination chair). A visible nystagmus (left or right) indicates failure of fixation suppression that is always central in origin. Gait is evaluated by asking patients to stand up and walk several steps forward and backward. The examining physician can qualitatively document ability to stand up without assistance, gait speed and stride length. The use of a high compliant foam pad to examine posture control is very helpful in “stressing” the system to evaluate postural sway, limits of stability and strategies (hip vs.

ankle sway). The examining physician should attempt to evaluate these parameters, as they are very helpful in addressing pathophysiology of falling and in tailoring appropriate vestibular rehabilitation programs. This is very critical in elderly patients who are evaluated for the primary complaint of falling. If the above exams are normal and the history is not specific for a primary ear or brain disease, hyperventilation for 2 minutes is helpful in identifying patients with "hyperventilation syndrome", particularly if it reproduces their own symptoms.

DIAGNOSTIC TESTS

Additional tests that are helpful in diagnosing ear problems include audiometry, vestibular tests, blood tests, CT and MRI. However, these tests need to be tailored according to the history and physical findings. Basic and advanced audiometry, especially if hearing loss and/or tinnitus are present, help narrow the diagnosis and tailor appropriate treatments. Vestibular testing with standard Electronystagmography (ENG or VNG) is helpful to confirm unilateral or bilateral vestibular loss and the presence of spontaneous and or positional nystagmus. It is seldom sensitive to abnormal eye movements which are best observed or video recorded during the physical examination. Vestibular evoked myogenic potentials (VEMP) are useful in evaluating the otolith organs. Advanced vestibular tests (chair and posturography) are helpful in selected patients who continue to have vestibular symptoms (i.e. incomplete central compensation) despite adequate treatment. It is not cost effective or medically indicated to obtain chair and posturography at the initial work up of the dizzy patient. Auditory brainstem response (ABR), Electro-Cochleography (ECoG), Otoacoustic emission (OAE) are helpful to confirm an inner ear diseases, to rule out central disease and to tailor and monitor treatments.

Screening blood tests for thyroid function, diabetes, lipids and autoimmune diseases are helpful in selected patients. Immune mediated inner ear tests which include ANA, ESR, RF and 68 KD western blot, are expensive and their yield is low.

Brain MRI scans are frequently "normal" in vestibular patients under the age of 50. Acoustic tumors and brain lesions that do not have clinical symptoms or signs on detailed vestibular and neurotological examinations are rare. The probability of an acoustic tumor in patients with unilateral hearing loss or tinnitus is less than ½ %. It is appropriate, therefore, to increase our threshold in ordering MRI studies in this patient population unless there are clear clinical signs and symptoms of brain disease. High-resolution CT scans are helpful when inner ear bony anomalies are suspected; for example large vestibular aqueduct or dehiscence of the superior semicircular canal.

Common disorders of Auditory and Vestibular Disorders

In general, the most common causes of hearing loss are presbyacusis and noise (industrial and recreational) induced hearing loss in adults and non syndromic hearing loss in children. Hearing loss due to chronic ear disease is declining because of the advent of antibiotics and allergy management. Sudden hearing loss[53;54], auditory neuropathy[55] and other types of central hearing loss are rare. The most common causes of peripheral vertigo and imbalance are vestibular neuritis, BPPV, Meniere's disease, and presbystasis. The most common cause of "central" dizziness is vestibular Migraine[56–58] and to a lesser extent hyperventilation induced dizziness. Other central causes include demyelination, acoustic tumors or cerebellar lesions. Central dizziness due to vertebrobasilar insufficiency (VBI) or vascular etiology in general, is uncommon. Isolated vertigo or dizziness is unlikely due to VBI unless other brainstem symptoms/signs and vascular risk factors exist. Disequilibrium of aging and gait disorders leading to falling are prevalent in the elderly population and are usually due to multi-sensory deficits involving vision, proprioception, hearing and vestibular functions.

Management of common Auditory and Vestibular disorders

Management should always be directed to underlying pathophysiology when possible. Age related hearing loss and noise induced hearing loss are usually treated with hearing aids, assistive listening devices and protection from noise and ototoxic medications when possible. Sudden hearing loss is commonly treated with oral and/or intratympanic steroids[59]. The yield is not particularly high but it continues to be the standard of practice in many countries. Congenital and hereditary hearing loss is commonly treated with hearing aids, cochlear implants or both. Auditory and speech rehabilitation is of critical importance in these cases[60]. Gene therapy of the human inner ear remains a future possibility given the existing knowledge and experience in animal studies[49;61]. The current treatments for tinnitus and auditory neuropathy remain empirical and are based on a mutimodalities approach.

Acute dizziness and vertigo is usually managed as an out-patient with vestibular suppressants (IM, IV or sublingual) and anti-emetic medications. Steroids can be used in selected patients. Vestibular suppressants should be used for a few days at most because they delay the brain's natural compensatory mechanism for peripheral vertigo. Recurrent BPPV is best treated with canalith repositioning maneuvers[62].

Acute vestibular neuritis is treated symptomatically and patients should start home or clinic based vestibular rehabilitation[44] as soon as possible to boost vestibular compensation. In general most patients experience significant resolution of symptoms with in 6–8 weeks. Meniere's disease or atypical BPPV should be considered in patients who continue to have imbalance and motion intolerance symptoms despite adequate trials of vestibular rehabilitation.

Meniere's disease first line of treatment is low salt and diuretics63. Vestibular suppressants can be used to abort exacerbations of vertigo. Intra-tympanic perfusion[64] of steroids or gentamicin is very effective in Meniere's disease. Steroids are used in early stages of the disease to stabilize hearing and control vertigo and gentamicin in late stages to control vertigo and Tumarkin drop attacks. It is important to provide early and aggressive treatment to hopefully bring hearing (mostly speech discrimination) to an "aidable" level, keeping in mind that these patients have a 25 % chance of developing Meniere's in the other ear.

Autoimmune inner ear disease [AIED]65;66 is commonly seen in middle age females. The typical presentation is bilateral, or unilateral, rapidly progressive sensorineural hearing loss with or without vertigo. It is usually associated with other autoimmune diseases, but it can be an isolated ear disease. Blood tests are available but they are not highly sensitive or specific. The history, audiometric and vestibular evaluations, absence of other diseases and positive response to steroids are the hallmarks of this disease. Generally, 1mg/kg/day (single dose, max 60mg/day) regimen is used for one month after which steroids are tapered slowly (with good response) or rapidly (with no response). Intratympanic steroids perfusion can be also used in these patients. Other immunosuppressive medications (e.g. Methotrexate) can be used as primary treatment or as steroid sparing medication67.

Vestibular Migraine[56;57] is treated with multimodal approach utilizing avoidance of triggers, prophylactic and abortive medications, and stress management. There are many options of medications such as triptans, anti anxiety, beta blockers, calcium channel blockers, antiepileptic medications and antidepressants. Sometimes it takes a trial and error approach to find out most effective approach. Critical to the management of vestibular migraine is not to use narcotics to avoid dependence and rebound effects.

Dysequilibrium of aging ("presbystasis"), gait disorders and consequent falling should be carefully evaluated for both intrinsic and extrinsic factors. Intrinsic causes include degenerative and neurological diseases especially multi-sensory deficits of vision, hearing and vestibular functions. Age related changes in gait and balance are subtle and may go unnoticed by patients and physicians. Appropriate sensory-motor integration of the three cardinal sensory modalities; vision, proprioception and vestibular, is critical for postural stability. The vestibular input is the least redundant and most conserved with aging. Therefore, the brain predominantly "looks" for the vestibular system for postural stability. Consequences of even mild forms of inner ear disease in the elderly are much more evident and serious as they can lead to falling. Early interventions to control inner ear disease and to start home based vestibular rehabilitation[44] are very critical in this population. Vestibular suppressants must be used sparingly. Most vestibular patients can effectively do home vestibular rehabilitation on their own. This is both convenient and cost effective especially in today's medical economics. In few selcted patients, occupational and physical therapy are helpful in addressing home safety, mechnical neck and postural problems that can impede vestibular rehabilitation, and to insure compliance with therapy.

Hyperventilation syndrome patients are treated with explanation of the diseases process and use of re-breathing exercises. Otherwise, additional cognitive therapy, stress management and medications are required.

Summary

Recent advances in the understanding of the auditory and vestibular systems are making it possible to more effectively manage their disorders. Thus, our insight into inner ear disease has significantly advanced with regard to the underlying cellular and molecular control of the fluid homeostasis in the ear, plasticity and compensatory mechanisms within the central vestibular pathways, and diagnostic protocols that isolate specific vestibular pathologies. This has ultimately led to better management of hearing and vestibular disorders because of our ability to target therapies to deal with disease, as well as symptoms. In view of the rapid research progress being made in all fields of otology, we anticipate many of these findings will dramatically improve our ability to effectively control, and reverse, the many ear disorders plaguing our society.

Acknowledgments

Supported by Grant Number R01 DC 05593 from the National Institute on Deafness and Other Communication Disorders, National Institutes of Health (Dr. Dennis Trune).

Reference List

1. Gabashvili IS, Sokolowski BH, Morton CC, Giersch AB. Ion channel gene expression in the inner ear. J Assoc Res Otolaryngol 2007;8:305–328. [PubMed: 17541769]
2. Hibino H, Kurachi Y. Molecular and physiological bases of the K+ circulation in the mammalian inner ear. Physiology (Bethesda) 2006;21:336–345. [PubMed: 16990454]
3. Lang F, Vallon V, Knipper M, Wangemann P. Functional significance of channels and transporters expressed in the inner ear and kidney. Am J Physiol Cell Physiol 2007;293:C1187–C1208. [PubMed: 17670895]
4. Trune, DR. Ion Homeostasis and Inner Ear Disease. In: Hamid SA, MA., editor. Medical Otology and Neurotology. A Medical Guide to Auditory and Vestibular Disorders. New York: Thieme; 2006. p. 21-23.
5. Huang D, Chen P, Chen S, Nagura M, Lim DJ, Lin X. Expression patterns of aquaporins in the inner ear: evidence for concerted actions of multiple types of aquaporins to facilitate water transport in the cochlea. Hear Res 2002;165:85–95. [PubMed: 12031518]

6. Beitz E, Zenner HP, Schultz JE. Aquaporin-mediated fluid regulation in the inner ear. Cell Mol Neurobiol 2003;23:315–329. [PubMed: 12825830]
7. Boone RT, Zuo C, Fan CY, Dornhoffer J. Modification of atrial natriuretic peptide receptor expression in the rat inner ear. Otol Neurotol 2005;26:534–537. [PubMed: 15891663]
8. Taguchi D, Takeda T, Kakigi A, Takumida M, Nishioka R, Kitano H. Expressions of aquaporin-2, vasopressin type 2 receptor, transient receptor potential channel vanilloid (TRPV)1, and TRPV4 in the human endolymphatic sac. Laryngoscope 2007;117:695–698. [PubMed: 17415141]
9. Weber PC, Cunningham CD III, Schulte BA. Potassium recycling pathways in the human cochlea. Laryngoscope 2001;111:1156–1165. [PubMed: 11568535]
10. Brandt N, Kuhn S, Munkner S, et al. Thyroid hormone deficiency affects postnatal spiking activity and expression of Ca2+ and K+ channels in rodent inner hair cells. J Neurosci 2007;27:3174–3186. [PubMed: 17376979]
11. Qu C, Liang F, Smythe NM, Schulte BA. Identification of ClC-2 and CIC-K2 chloride channels in cultured rat type IV spiral ligament fibrocytes. J Assoc Res Otolaryngol 2007;8:205–219. [PubMed: 17334850]
12. Lee JH, Marcus DC. Purinergic signaling in the inner ear. Hear Res 2008;235:1–7. [PubMed: 17980525]
13. Lalwani AK, Castelein CM. Cracking the auditory genetic code: nonsyndromic hereditary hearing impairment. Am J Otol 1999;20:115–132. [PubMed: 9918184]
14. Nance WE. The genetics of deafness. Ment Retard Dev Disabil Res Rev 2003;9:109–119. [PubMed: 12784229]
15. Van Laer L, Cryns K, Smith RJ, Van Camp G. Nonsyndromic hearing loss. Ear Hear 2003;24:275–288. [PubMed: 12923419]
16. Spicer SS, Schulte BA. Evidence for a medial K+ recycling pathway from inner hair cells. Hear Res 1998;118:1–12. [PubMed: 9606057]
17. Chiba T, Marcus DC. Nonselective cation and BK channels in apical membrane of outer sulcus epithelial cells. J Membr Biol 2000;174:167–179. [PubMed: 10742460]
18. Jentsch TJ. Neuronal KCNQ potassium channels: physiology and role in disease. Nat Rev Neurosci 2000;1:21–30. [PubMed: 11252765]
19. Chang EH, Van Camp G, Smith RJ. The role of connexins in human disease. Ear Hear 2003;24:314–323. [PubMed: 12923422]
20. Couloigner V, Sterkers O, Ferrary E. What's new in ion transports in the cochlea? Pflugers Arch 2006;453:11–22. [PubMed: 16773381]
21. Nickel R, Forge A. Gap junctions and connexins in the inner ear: their roles in homeostasis and deafness. Curr Opin Otolaryngol Head Neck Surg 2008;16:452–457. [PubMed: 18797288]
22. Yan D, Liu XZ. Cochlear molecules and hereditary deafness. Front Biosci 2008;13:4972–4983. [PubMed: 18508562]
23. Spiess AC, Lang H, Schulte BA, Spicer SS, Schmiedt RA. Effects of gap junction uncoupling in the gerbil cochlea. Laryngoscope 2002;112:1635–1641. [PubMed: 12352678]
24. Cohen-Salmon M, Regnault B, Cayet N, et al. Connexin30 deficiency causes instrastrial fluid-blood barrier disruption within the cochlear stria vascularis. Proc Natl Acad Sci U S A 2007;104:6229–6234. [PubMed: 17400755]
25. Takeuchi S, Ando M. Dye-coupling of melanocytes with endothelial cells and pericytes in the cochlea of gerbils. Cell Tissue Res 1998;293:271–275. [PubMed: 9662649]
26. Tadros SF, Frisina ST, Mapes F, Frisina DR, Frisina RD. Higher serum aldosterone correlates with lower hearing thresholds: a possible protective hormone against presbycusis. Hear Res 2005;209:10–18. [PubMed: 16039078]
27. Trune DR, Kempton JB, Gross ND. Mineralocorticoid receptor mediates glucocorticoid treatment effects in the autoimmune mouse ear. Hear Res 2006;212:22–32. [PubMed: 16307853]
28. Kim SH, Kim KX, Raveendran NN, Wu T, Pondugula SR, Marcus DC. Regulation of ENaC-mediated sodium transport by glucocorticoids in Reissner's membrane epithelium. Am J Physiol Cell Physiol 2009;296:C544–C557. [PubMed: 19144862]

29. Trune DR BK. Blocking the glucocorticoid receptor with RU-486 does not prevent glucocorticoid restoration of autoimmune mouse hearing loss. Audiology & Neurotology. 2009 In Press.
30. Wangemann P. Comparison of ion transport mechanisms between vestibular dark cells and strial marginal cells. Hear Res 1995;90:149–157. [PubMed: 8974992]
31. Sage CL, Marcus DC. Immunolocalization of ClC-K chloride channel in strial marginal cells and vestibular dark cells. Hear Res 2001;160:1–9. [PubMed: 11591484]
32. Milhaud PG, Pondugula SR, Lee JH, et al. Chloride secretion by semicircular canal duct epithelium is stimulated via beta 2-adrenergic receptors. Am J Physiol Cell Physiol 2002;283:C1752–C1760. [PubMed: 12388054]
33. Curthoys IS. Vestibular compensation and substitution. Curr Opin Neurol 2000;13:27–30. [PubMed: 10719646]
34. Paterson JM, Menzies JRW, Bergquist F, Dutia MB. Cellular mechanisms of vestibular compensation. Neuroembryology and Aging 2006;3:3183–3193.
35. Paterson JM, Short D, Flatman PW, Seckl JR, Aitken A, Dutia MB. Changes in protein expression in the rat medial vestibular nuclei during vestibular compensation. J Physiol 2006;575:777–788. [PubMed: 16825307]
36. Seemungal BM, Gresty MA, Bronstein AM. The endocrine system, vertigo and balance. Curr Opin Neurol 2001;14:27–34. [PubMed: 11176214]
37. Lindsay L, Liu P, Gliddon C, Zheng Y, Smith PF, Darlington CL. Cytosolic glucocorticoid receptor expression in the rat vestibular nucleus and hippocampus following unilateral vestibular deafferentation. Exp Brain Res 2005;162:309–314. [PubMed: 15580339]
38. Zhang R, Smith PF, Darlington CL. Immunocytochemical and stereological study of glucocorticoid receptors in rat medial vestibular nucleus neurons and the effects of unilateral vestibular deafferentation. Acta Otolaryngol 2005;125:1258–1264. [PubMed: 16303671]
39. Guilding C, Seckl JR, Dutia MB. 11Beta-hydroxysteroid dehydrogenase type 1 activity in medial vestibular nucleus and cerebellum after unilateral vestibular deafferentation in the rat. Stress 2004;7:127–130. [PubMed: 15512857]
40. Gliddon CM, Smith PF, Darlington CL. Interaction between the hypothalamic-pituitary-adrenal axis and behavioural compensation following unilateral vestibular deafferentation. Acta Otolaryngol 2003;123:1013–1021. [PubMed: 14710901]
41. Kitahara T, Kondoh K, Morihana T, et al. Steroid effects on vestibular compensation in human. Neurol Res 2003;25:287–291. [PubMed: 12739240]
42. Johnston AR, Seckl JR, Dutia MB. Role of the flocculus in mediating vestibular nucleus neuron plasticity during vestibular compensation in the rat. J Physiol 2002;545:903–911. [PubMed: 12482895]
43. Strupp M, Arbusow V, Brandt T. Exercise and drug therapy alter recovery from labyrinth lesion in humans. Ann N Y Acad Sci 2001;942:79–94. [PubMed: 11710505]
44. Hamid, M.; Samy, H. Vestibular and Balance Rehabilitation. In: Hamid, M.; Sismanis, A., editors. Medical Otology and Neurotology. A Clinical Guide to Auditory and Vestibular Disorders. New York: Thieme; 2006. p. 94-101.
45. Brigande, JV. Regenerative Medicine for Inner Ear Disease. In: Hamid SA, MA., editor. Medical Otology and Neurotology. A Medical Guide to Auditory and Vestibular Disorders. New York: Thieme; 2006. p. 33-42.
46. Snoecks, RL.; Van Camp, G. Nonsyndromic hearing loss: cracking the cochlear code. In: Martini A, SDRA., editor. Genes, Hearing, and Deaafness: From Molecular Biology to Clinical Practice. London, UK: Informa; 2007. p. 63-90.
47. Rubel EW, Oesterle EC, Weisleder P. Hair cell regeneration in the avian inner ear. Ciba Found Symp 1991;160:77–96. [PubMed: 1752172]
48. Diensthuber M, Oshima K, Heller S. Stem/progenitor cells derived from the cochlear sensory epithelium give rise to spheres with distinct morphologies and features. J Assoc Res Otolaryngol 2009;10:173–190. [PubMed: 19247714]
49. Kesser BW, Lalwani AK. Gene therapy and stem cell transplantation: strategies for hearing restoration. Adv Otorhinolaryngol 2009;66:64–86. [PubMed: 19494573]

50. McCullar JS, Oesterle EC. Cellular targets of estrogen signaling in regeneration of inner ear sensory epithelia. Hear Res 2009;252:61–70. [PubMed: 19450430]
51. Fu Y, Wang SQ, Wang JT, Wang GP, Xie J, Gong SS. Experimental study on embryonic neural stem cells transplantation into natural rat cochlea via round window. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 2008;43:944–949. [PubMed: 19141249]
52. Hamid, M.; Sismanis, A. Clinical Approach to Patients with Auditory and Vestibular Disorders. In: Hamid, M.; Sismanis, A., editors. Medical Otology and Neurotology. A Clinical Guide to Auditory and Vestibular Disorders. New York: Thieme; 2006. p. 43-63.
53. Lazarini PR, Camargo AC. Idiopathic sudden sensorineural hearing loss: etiopathogenic aspects. Rev Bras Otorrinolaringol (Engl Ed) 2006;72:554–561.
54. Narozny W, Kuczkowski J, Kot J, Stankiewicz C, Sicko Z, Mikaszewski B. Prognostic factors in sudden sensorineural hearing loss: our experience and a review of the literature. Ann Otol Rhinol Laryngol 2006;115:553–558. [PubMed: 16900810]
55. Bamiou DE, Musiek FE, Luxon LM. Aetiology and clinical presentations of auditory processing disorders--a review. Arch Dis Child 2001;85:361–365. [PubMed: 11668093]
56. Lempert T, Neuhauser H, Daroff RB. Vertigo as a symptom of migraine. Ann N Y Acad Sci 2009;1164:242–251. [PubMed: 19645907]
57. Neuhauser H, Lempert T. Vestibular migraine. Neurol Clin 2009;27:379–391. [PubMed: 19289221]
58. Neuhauser HK. Epidemiology of dizziness and vertigo. Nervenarzt 2009;80:887–894. [PubMed: 19626307]
59. Sismanis A. Diagnostic and management dilemma of sudden hearing loss. Arch Otolaryngol Head Neck Surg 2005;131:733–734. [PubMed: 16103309]
60. Baldassari CM, Schmidt C, Schubert CM, Srinivasan P, Dodson KM, Sismanis A. Receptive language outcomes in children after cochlear implantation. Otolaryngol Head Neck Surg 2009;140:114–119. [PubMed: 19130973]
61. Pfister, M.; Lalwani, AK. Gene therapy of the inner ear. In: Martini A, SDRA., editor. Genes, Hearing, and Deaafness: From Molecular Biology to Clinical Practice. London, UK: Informa; 2007. p. 299-304.
62. Hamid MA. The Maneuvers for BPPV. Operative Techniques in Otolaryngology-Head and Neck Surgery 2001;12:148–150.
63. Hamid MA. Meniere's disease. Pract Neurol 2009;9:157–162. [PubMed: 19448058]
64. Hamid M, Trune D. Issues, indications, and controversies regarding intratympanic steroid perfusion. Curr Opin Otolaryngol Head Neck Surg 2008;16:434–440. [PubMed: 18797285]
65. Hughes GB, Barna BP, Kinney SE, Calabrese LH, Hamid MA, Nalepa NJ. Autoimmune endolymphatic hydrops: five-year review. Otolaryngol Head Neck Surg 1988;98:221–225. [PubMed: 3127786]
66. Garcia-Berrocal JR, Ramirez-Camacho R, Trinidad A. Autoimmune hearing loss: improving diagnostic performance. Acta Otorrinolaringol Esp 2007;58:138–142. [PubMed: 17428409]
67. Salley LH Jr, Grimm M, Sismanis A, Spencer RF, Wise CM. Methotrexate in the management of immune mediated cochleovesitibular disorders: clinical experience with 53 patients. J Rheumatol 2001;28:1037–1040. [PubMed: 11361185]