Clinical Physiology of the

VESTIBULAR SYSTEM

Module 1

Genx A DIVISION OF HETERO HEALTHCARE

DEFEAT DIZZINESS

Dr. Anirban Biswas

For the Use of a Registered Medical Practitioner, Hospital or a Laboratory Only

Contents

Preface

I once had the good fortune of attending a master class on Vestibular Physiology by Prof. David Zee, a neurologist from John Hopkin's University in the US with special interest in ataxia, imbalance and vestibular disorders. I regard and respect him as one of the most knowledgeable clinicians in neurotology. He began his lecture saying *"pretend you are a first year medical student, wide awake, eager to learn, ready to accept new ideas, and still remember some high school physics and math. Forget how medical school taught you to memorize rather than think. Put on your thinking cap and enjoy a roller coaster ride through vestibular physiology. It will pay off in your clinics".* Nothing can be truer and a better intro to the Physiology of the Maintenance of Balance. And this is how I would also like to introduce this complex subject to clinicians who have ventured to unravel the mystery that underlies the fascinating discipline of clinical neurotology.

The maintenance of balance is possibly the most complicated biological mechanism in the human body. It has deep ramifications in different parts of the body from head to foot and involves the central and peripheral nervous systems, the psychic system and cognitive systems, the musculoskeletal system, the vestibular system and organs like the brain, the ears and the eyes. Each one of these systems and the organs that comprise them vies with the other in respect of the complexities of the structure and function that is packed into them. No wonder most clinicians fight shy of this part of the medical curriculum. This is a subject that medical teachers seldom teach and medical students hardly ever study. Thirty years back when I was a medical student, our seniors assured us that we can safely skip this portion as the examiner also was equally confused and would not dare ask a question on vestibular physiology lest the examiner's ignorance got exposed. Our junior colleagues tell us that the same state of affairs prevails today also.

However, so much of advancements have taken place in neurotology especially in the diagnostics and therapeutics of balance disorders, that clinicians involved in handling balance disorder patients do not afford to stay oblivious to the biological mechanism of the maintenance of balance now. Without a very clear understanding of the the physiology of maintenance of balance, clinicians cannot have a thorough grasp on the interpretation of the modern vestibulometric tests and the different therapeutic modalities that are now prevalent. Hence this (daunting) endeavour of trying to present to clinicians a very brief glimpse of the back-office activities that go on relentlessly every moment of our lives to ensure that we are physically, visually and perceptually stable. Defects in the structure or function of the balance organs induce inadequacies of physical/ visual/ perceptual stability which in turn jeopardize mental stability and severely compromises quality of life and peace of mind too. A feeling of instability or a sensation of the visual surroundings moving and fear of losing balance is as much traumatic physically as it is mentally.

I am deeply indebted to Hetero Healthcare for printing and distributing this small booklet to clinical practitioners and especially to Mrs. Sheetal Pandit and Ashish Padelkar for their constant prodding, help and support without which this venture would not have materialized. I am also extremely grateful to Dr. Shrikant Deshmukh, neurologist from Aurangabad and to Dr. Pushkar Kasat, neurotologist from Mumbai both of whom have worked with me for a pretty long time in my clinic in Kolkata trying to learn the nuances of neurotology and have been a major help in correcting and editing the manuscript. This small booklet is dedicated to both of them in remembrance of the wonderful time we spent together learning from each other and sharing our mutual ignorance(s).

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Overview

The maintenance of balance is a very complex biological mechanism. But it works very logically and according to set principles; hence understanding and unraveling this so-called 'complex' mechanism is not difficult for anyone with a logical and analytical mind. The Central Nervous System (CNS) collects information about the static and dynamic position of the body in relation to the ground and the surroundings from certain sensors in different parts of the body. From these sensors the brain comes to know not only about the external environment i.e., (1) the stability of the ground where we are positioned (e.g., where we are standing/ sitting/ lying or the surface where we are walking/ running/ skating / climbing etc.) and about (2) the stability of the surroundings, but also about (3) the stability and position of the internal environment i.e., how the body is positioned in relation to the surrounding three dimensional space and the relative positions of the body parts like how is the head positioned on the shoulders. Information from different sensors is first collected and then integrated in the brain. Once this is done, the brain is fully informed about the stability of the subject's position and that of the physical environment around the subject. After the brain has this information, it hunts for a similar situation in the vestibular memory where there is a store of the individual's past experiences. So whenever the brain is getting information about the stability of the ground and the surroundings, the brain is also retrieving information from the vestibular memory about similar conditions of stability of the ground and the surroundings, from the past and it compares and combines them and then formulates a particular motor output by which the body's balance is best maintained in that particular situation. This signifies that we have to have (1) an efficient system of storing information in vestibular memory and also (2) that for retrieving the requisite information pertaining to a similar balance situation from the vestibular memory as and when required. This in turn means that there is a huge a part played by the cognitive system. The more efficacious the cognitive system is, the better is the efficiency of storing information (i.e., learning) related to a particular vestibular challenge in the vestibular memory and better is the faculty of

retrieval of stored information of a similar situation from the vestibular memory. If someone has a more efficient cognitive faculty (to put it more simply, better intellectual powers) then he/ she will be storing in and retrieving information from the vestibular memory of the brain much more efficiently than another person who has poorer cognitive powers. Balance faculties of different persons are different because the cognitive skills are different in different individuals. Similarly, cognitive skill of a 75 year old person cannot be compared to that of a 30 year old person. All these have to be taken into account and factored in when we are discussing about the mechanism of maintenance of balance in a clinical setting.

Maintenance of Balance

CNS collects information about static/ dynamic position of the body in relation to the ground and the surroundings from certain sensors in different parts of the body

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Information from different sensors integrated in the brain and compared with previously stored experiences

↓

A very precise, coordinated and accurately timed ***motor output generated reflexly*** which contracts some specified muscles and maintains or restores balance

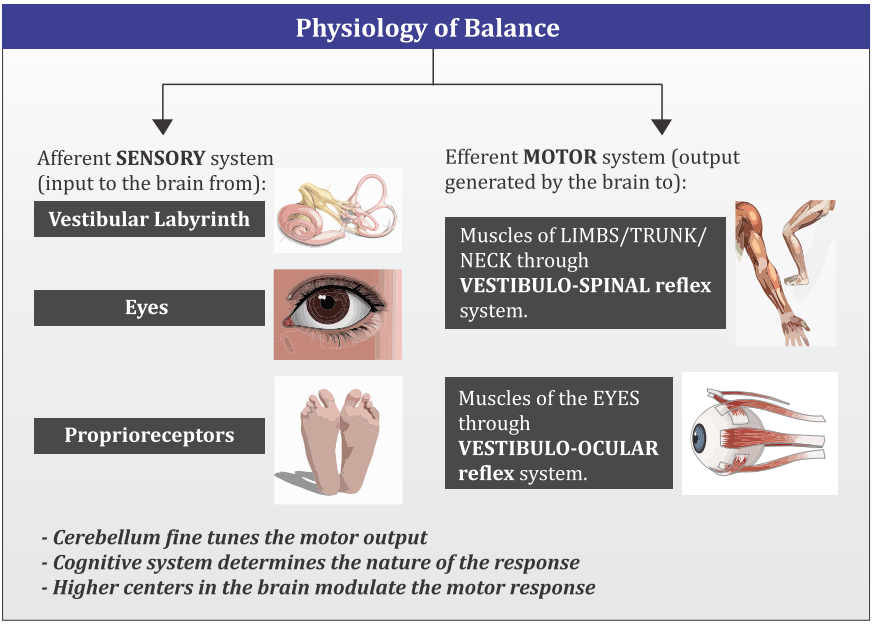
Information to the brain about the stability of the ground and the surroundings and the physical orientation of the body is collected from three types of sensors:

i) Vestibular labyrinths in the ears, which is one of the most complex organs of the body. The vestibular labyrinths basically sense different types of body movements in different planes and inform the brain about the individual's position in respect to the ground and the surroundings and about the spatial orientation i.e., up-down movement, forward-backward or side to side movement, any rotatory/ angular movement etc. All these information is collected by the vestibular labyrinths and sent to the brain through the vestibular nerve. The vestibular labyrinths are the internal sensors of the balance system as they sense the individual's static (when the individual is stationary) and dynamic (when the individual is in motion) positions. The other two sensors i.e., the eyes and the proprioceptors described below are the external sensors as they sense the stability and position of the surrounding environment.

ii) The eyes inform the brain about the stability of the surroundings, whether the visual environment is stable or is moving.

iii) Proprioceptors in the soles of the feet, in the buttocks, in the back, which inform the brain about the stability of the ground and the surroundings where we are standing/ sitting / lying. Even if we are lying down or standing at a 2° inclined plane, the brain can sense this with the help of the proprioceptors.

On the basis of the information obtained from these three different sensors, the brain will evolve a motor output by virtue of which it will cause a very precise and accurately calculated contraction of certain specified body muscles by which the body's balance is maintained *(Ref. Biswas Anirban. Vertigo and what is new in it from the general physician's perspective In Kamath S (Ed.) Medicine Update. 2017; 22:586-591).* If the subject is tilting 15° to the right, the muscles of the left side of the body will reflexly contract in such a manner that there will be an exact 15° correction and this correction will never be a 14.5° correction or a 15.5° correction so that the subject becomes perfectly erect. There is never any under-correction or any over-correction.



The motor output evolved by the brain is directed to two groups of muscles viz.:-

1) The muscles of the body (limbs and trunk) i.e., the skeletal muscles:

If the brain senses that the body is tilting towards the left side then immediately the brain will cause contraction of the muscles of the right side of the body to make it erect and restore stability ***(Fig 1).*** This correction of the body posture is always a very accurate and precise 100% correction. The motor output is fine-tuned by the cerebellum. The cerebellum calculates which muscles to contract, how much of contraction, in what order and for what period of time. The cerebellum ensures that there is never any under-correction or any over-correction. For maintenance of perfect balance this accurate 100% correction is very important.

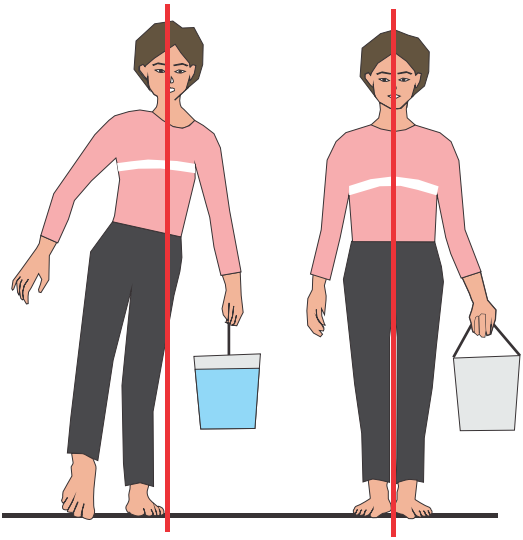


Fig 1. Compensated Posture for maintenance of balance.

2) The external muscles of the eyes i.e., the extra-ocular muscles:

Why did nature choose these miniscule muscles of the eyes for maintenance of balance? An example will clarify this. Supposing I am standing still looking at a car 30 feet in front of me. As I am looking at the car, the image

of the car will be cast on my retina, not on the entire retina, but on the most sensitive part of the retina, the 'fovea' which is the point in the retina with the greatest number of photo-receptor cells and highest visual acuity.A visual object is seen most clearly and stably if the image of the object is fixed in the fovea. Now if I move my head or the car starts moving, thenthe image will slip out from the fovea to the less sensitive parts of the retina (termed as 'retinal slip' in medical parlance), and when this happens there will be blurring of vision and a drop of visual acuity which the brain will feel as a sense of motion, the subject will feel vertiginous and will get a sensation that the visual surroundings are moving. This happens as there is a sensory conflict. The vestibular system has different sensors; all of them should send identical information to the brain. Otherwise the brain will get confused. When the different sensors send contradictory information then it is called a 'sensory conflict'. Usually the brain is smart enough to identify which input is correct and which input is to be ignored and intelligently acts on the more relevant information. But not always.

Let us assume a situation where I am standing at a place without any head movement and looking at a car which was standing but has suddenly started moving forward from the right side of my visual field to the left side. I am standing erect at a stable place without movement and so my proprioceptors in the soles of the feet are informing the brain that everything is stable, my head is not moving and so the vestibular labyrinths are informing the brain that everything is stable but when the car starts moving, the eyes are informing the brain that there is movement. This is called a sensory conflict as the vestibular inputs are sending contradictory information to the brain. So the brain is bound to get confused and the result of this is a balance disorder i.e., feeling vertiginous and unsteady, especially the former.

But day in and day out we are seeing moving things while we are standing or sitting on a fixed stable place but do not feel vertiginous. Why? Because we have a very smart and efficient vestibular system. As soon as the car starts moving, the extra-ocular muscles will contract in such a way that as the car starts moving the subject's eyes will also move at the same speed at which the car is moving such that the image of the moving car will remain fixed in the fovea and there will be no retinal slip (i.e., no slippage of the image of the car in the subject's retina) whatsoever.

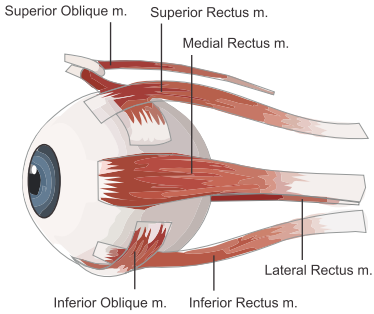
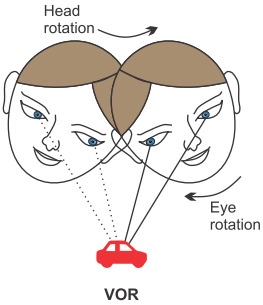


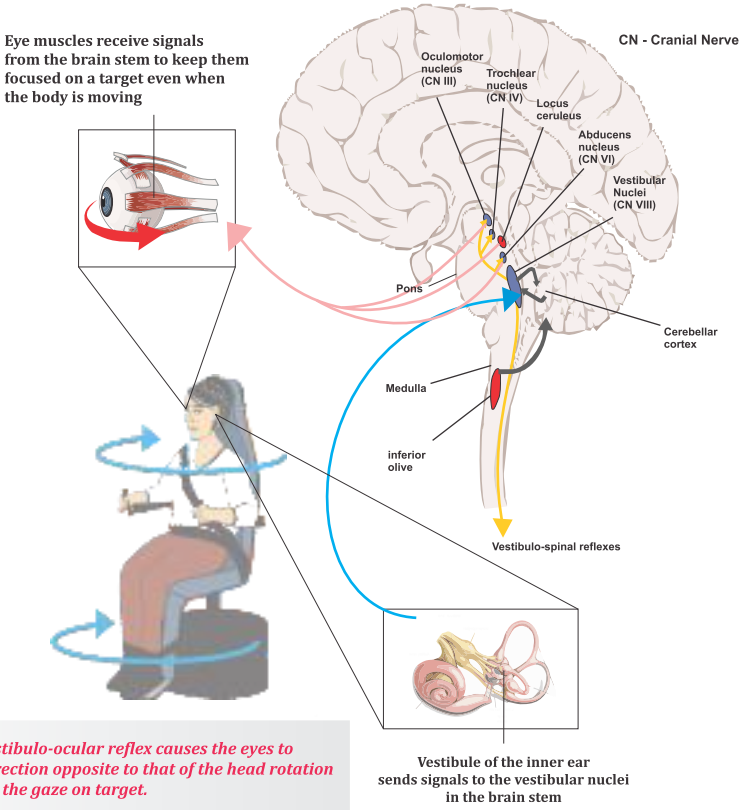
Fig 2. Extra-Ocular Muscles.



This stabilization of the image of the car in the fovea is effected by contraction of the six extra-ocular muscles namely the lateral, medial, inferior and superior rectus, and the inferior and superior oblique muscles ***(Fig 2)***.

These extra-ocular muscles will contract in a very precise way such that the image will remain fixed in fovea and there will be no retinal slip whatsoever. If there is any retinal slip, the subject will feel vertiginous. Here also the cerebellum will decide and control how much each extra-ocular muscle will contract and at what extent, for what duration of time and in what order.

In an opposite situation, when the subject is standing at a stable place (i.e., the proprioceptors are informing the brain that the ground is stable and that there is no movement) and looking at a car which too is stationary (i.e., the eyes are informing the brain that the surroundings are stable), if the subject suddenly moves the head from the left to the right, the vestibular labyrinths will be stimulated and will inform the brain that there is movement. This will lead to contradictory information reaching the brain (the proprioceptors and eyes informing the brain that everything is stable but the vestibular labyrinths informing the brain that there is movement) causing a sensory conflict. There will also be a retinal slip as the image of the car will slip out of the fovea to the less sensitive parts of the retina. This is again bound to generate the sensation of vertigo and unsteadiness, but that too does not happen in normal persons as we have a very effective and efficient vestibular system that senses the head movement and brings about a movement of the eyes in the opposite direction (i.e, the eyes will move from the right to left as the subject has moved the head from left to right) in the same speed as that of the head movement ensuring thereby that the image of the car remains fixed in the



The (VOR) vestibulo-ocular reflex causes the eyes to rotate in a direction opposite to that of the head rotation in order to fix the gaze on target.

Fig 3. The Vestibulo-ocular reflex system.

fovea and there is no retinal slip whatsoever. The vestibular labyrinths can sense any head movement and send the information about the nature of head movement to the oculomotor system (the part of the central nervous system that executes eye movement) which in turn effectively moves the eyes such that there is no retinal slip of images in the fovea whenever we move our head in any direction and also when we see moving objects ***(Fig 3).*** Stabilization of gaze is one of the main functions of the balance system and is achieved by many systems viz. the vestibular, the ocular and the oculo-motor systems working in tandem. It is for this mechanism of gaze stabilization that we can read street signs while walking or when sitting in a moving car. A person with a bilateral vestibulopathy (i.e., dysfunctional vestibular labyrinth on both sides) will have to stop walking or stop the car to read the street signs.

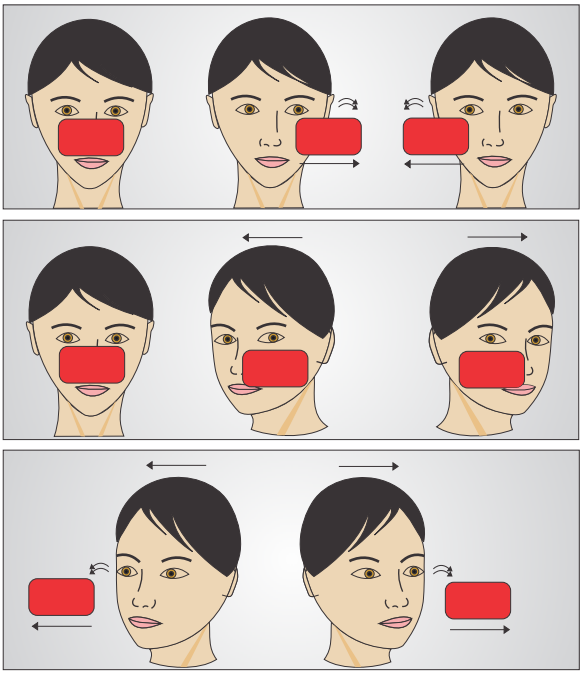


Fig 4. FUNCTIONS OF VESTIBULO-OCULAR REFLEX (VOR)

Maintaining the gaze stabilization when:

Fig 4 (A). The visual target moves but the head is steady.

Fig 4 (B). The head moves but the visual target is steady.

Fig 4 (C). Both the head as well as the visual target are moving together.

The function of the vestibulo-ocular reflex is to prevent any retinal slip and keep images of objects in the visual field firmly anchored in the fovea when;

(a) the head is stable but the visual field is moving,
(b) the head moves but the visual surroundings are stable, and
(c) both the visual field as well as the head are moving ***(Fig 4).***

Any retinal slippage of the visual images from the fovea will not only cause a vertiginous sensation, it will also cause a sharp drop in the visual acuity. The Dynamic Visual Acuity test, one of the common vestibulometric tests evaluates functional integrity of the vestibulo-ocular reflex and thereby indirectly the functional status of the semicircular canals of the vestibular labyrinths by documenting any abnormal drop in visual acuity on fast head movement. It is known from published studies that if a visual image slips out by as little as 2 degrees from the fovea, the visual acuity drops by 50%. *(R J Jacobs, Visual resolution and Contour interactions in the fovea and periphery published in Vision Research 1979; and R H Carpenter 1091)*

Motor Mechanisms of the Vestibular System

The body muscles contract by a reflex system called the **Vestibulo-Spinal Reflex System (VSR)** and the eye muscles contract by a reflex system known as **Vestibulo-Ocular Reflex System (VOR)**. These are the two reflex systems which actually maintain our body's balance.

The cerebellum fine tunes the motor output i.e., how much each muscle will contract and for what length of time as already explained. The cognitive system determines the nature of the response. The cognitive system retrieves from the vestibular memory a similar situation and determines that under a particular situation what will be the best outcome (motor response). If the cognitive system is smart enough then it will give a very correct direction to the motor system, such that with the minimum amount of effort, the best possible results can be achieved. Next, the higher centers in the brain will modulate the motor response because the neural signals to the muscles of the limbs and the trunk as well as that to the eyes will traverse from the motor cortex of the brain passing through different stations in the brain like the internal capsule, thalamus, basal ganglia, reticular formation etc. These structures are the relay stations of the neural signals carried down from the motor cortex to the relevant muscles and each of these relay stations has some function in modulating the motor response ***(Fig 5).***

Defects in any of these structures will jeopardize the body's balance. A very basic idea of the motor pathways from the motor cortex in the cerebrum to the motor nuclei of the eye muscles and that to the anterior horn cells of the spinal cord for movement of the voluntary muscles of the limbs and trunk is very important for the clinician handling patients of balance disorders.

Parts of the CNS majorly involved in the motor output for maintenance of balance

- **Pyramidal and Extra-pyramidal Tracts**
- **Basal Ganglia**
- **Reticular Formation**
- **Thalamus**
- **Cerebellum**
- **Ascending/ descending tracts in spinal cord**

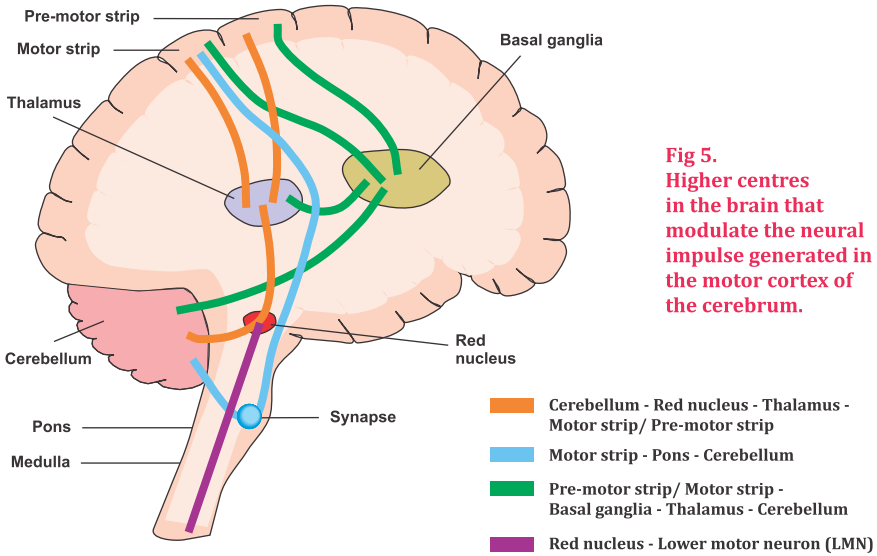


Fig 5.
Higher centres in the brain that modulate the neural impulse generated in the motor cortex of the cerebrum.

The connections between the motor cortex in the forebrain and motor neurons within the brainstem that houses the motor nuclei of the nerves for eye movement (the midbrain of the brainstem has the nuclei of the oculomotor nerve (Cr.nv-III) and trochlear nerve (Cr.nv-IV) the pons has the nuclei of the abducens nerve (Cr.nv-VI)) and the spinal cord (that houses the anterior horn cells for movement of the skeletal muscles of the limbs and trunk) are made up of two tracts or systems viz.:
(1) The pyramidal system and (2) The extra-pyramidal system. These tracts are concerned with the different motor activities of the body and any defect in these tracts leads to abnormalities in the execution of any motor activity i.e. in the movement of the body parts.

The Pyramidal System

Pyramidal system is the pathway for direct activation of the skeletal muscles in the limbs and the trunk. All of the motor impulses emanated from the cerebral cortex of brain (also called motor cortex) travel through this tract. This pathway supplies the voluntary muscles of the head, neck and limbs. Neurons of this tract originate in the post-central gyrus or primary motor cortex. The voluntary muscles are the skeletal muscles of the head, the limbs and the trunk. This neural network from the motor area of the cerebral cortex down to the motor nucleus of the cranial

nerves as well as to the anterior horn cells in the spinal cord is called pyramidal pathway as the tract passes through two pyramid like structures in the ventral (i.e., anterior) part of the midline at the medulla.

The pyramidal system has two tracts: ***cortico-bulbar tract*** and ***cortico-spinal tract.*** The cortico - bulbar tract originates in the motor cortex in the pre-central gyrus of the cerebral cortex in the brain and descends to the genu of the internal capsule and then enters the basilar part of the pons and finally terminate in the motor nuclei of the cranial nerves of the opposite side ***(Fig 6)***. These fibers are responsible for the motor activity of the head neck muscles which includes the extra-ocular muscles of the eyes that execute eye movement and are hence very important in the control of gaze stabilization which is a primary function of the vestibular system. Any defect in the cortico-bulbar tracts or in the genu of the internal capsule will hence lead to abnormalities in gaze stabilization and cause vertigo.

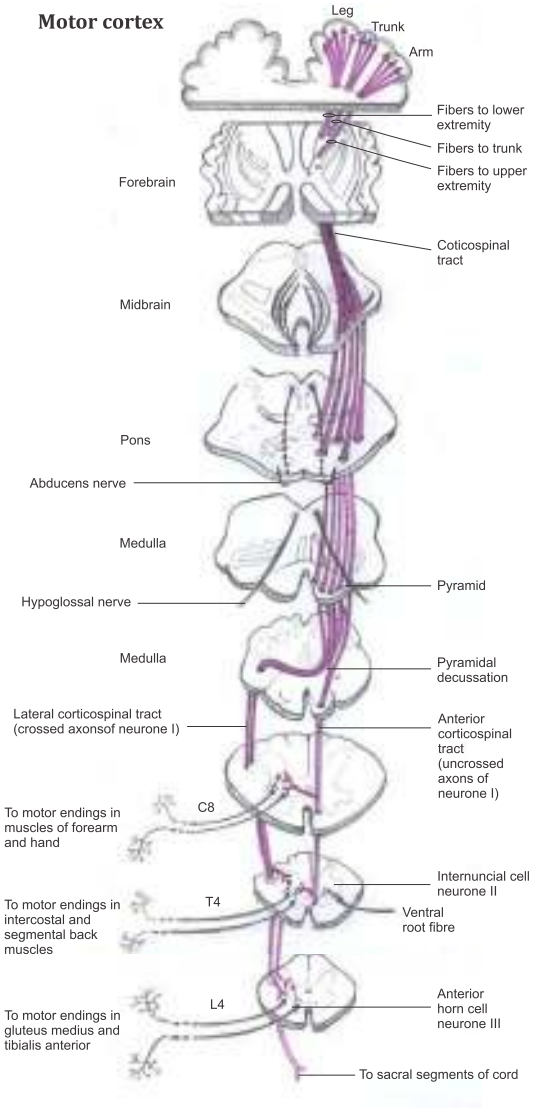


Fig 6. Pathway of cortico-spinal tracts. The pyramidal system.

The nerve fibers of the cortico-spinal tract originate in the motor area of the cerebral cortex (primary motor area, the pre motor area, and the supplementary motor area of the frontal lobe) travels down through the coronaradiata, posterior half of lateral ventricle, posterior limb of internal capsule, then enters the midbrain through cerebral peduncle, and after that to the medulla where they form medullary pyramids on either side of midline. After this most fibers of the cortico-spinal tract decussate i.e., cross over to the other side and descend in the contralateral side of the spinal cord as the lateral cortico-spinal tract and synapse (i.e., terminate) at the anterior horn cells. From the anterior horn cells the next neurons start and through the peripheral motor nerves reach the muscles of the limbs and trunk, mainly the limbs. Some fibers do not decussate at the level of the medulla and travel downwards through the spinal cord as the anterior cortico-spinal tract and decussate lower down in the spinal cord and mostly supply the trunkal muscles.

In its passage from the motor cortex to the final destination which is the skeletal muscles, the cortico-spinal tracts pass through some relay stations in the brain like the thalamus. The final activity of motor neurons is hence a result of activity, within the cerebral cortex and/ or thalamus. The thalamus effectively acts as a relay station from the cerebrum and cerebellum before neurons enter the motor pathways of the spinal cord. Disorders of the thalamus will hence lead to erroneous/ faulty muscular contraction, as a malfunctioning thalamus will abnormally change the motor output that has originated in the cerebral motor cortex. Any defect in the entire pathway right from the cerebral motor cortex to the skeletal muscles as well as that in the relay stations will cause defective contraction of the muscles of the limbs/ trunk and lead to postural instability. Hence to maintain erect posture and to prevent a fall this cortico-spinal tract has to be perfectly functional and any defect in the pathway or in the relay stations will lead to imbalance. Hence, the functional integrity of the relay systems like the thalamus also needs to be evaluated in patients presenting with imbalance.

Signs of Disorder in the Pyramidal Tract

- *Areflexia*
- *Hyper-reflexia*
- *Abnormal Babinsky reflex*
- *Hypotonia*
- *Hypertonia*

Extrapyramidal System

The descending fibers from the cerebral motor cortex other than that by the pyramidal tracts are known as the extra pyramidal tracts. Extrapyramidal tracts are responsible for maintenance of postural balance as well as control of movement of the eyes. They exerts an inhibitory control over the lower centers and by modifying neural impulses that originates in the cerebral cortex they fine tune the involuntary movements. Impulses generated at the primary motor cortex areas are sent via the extrapyramidal fibers to the basal ganglia ***(Fig 7)***. These tracts are in turn modulated by various parts of the central nervous system, including the nigrostriatal pathway, the basal ganglia, the cerebellum, the vestibular nuclei, and different sensory areas of the cerebral cortex. Maintenance of balance especially that of postural balance involves coordinated movement of groups of muscles in a very precise and controlled fashion; defects in the extra-pyramidal tracts jeopardize this coordination of groups of muscles and results in imbalance. Hence evaluation of the extrapyramidal system is very important when examining a balance disorder patient.

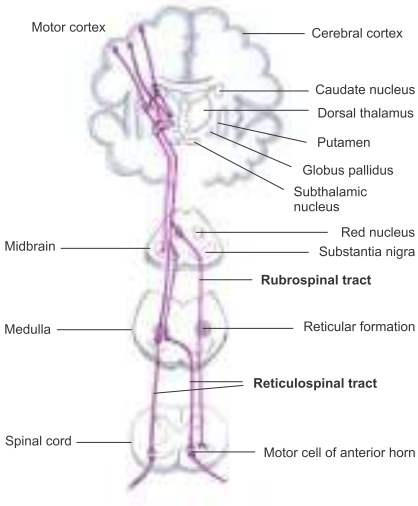


Fig 7. The extrapyramidal system.

Signs of Extrapyramidal Tract Disorder

- *Resting tremor (4-8 Hz frequency)*
- *Posture (hunched over)*
- *Slow monotonal speech*
- *Expressionless facial expression*
- *Siallorhoea (i.e.: drooling), due to bradykinesia of swallowing.*
- *Fine eyelid tremor - when closing eyes*
- *Muscular – bradykinesia, rigidity, hypotonia and low frequency tremors.*
- *Gait - Difficulty initiating and stopping movements, 'Shuffling gait' with small steps, Leaning forwards to initiate movement, festinate gait (starting slow and speeding up as they continue to walk), etc.*

The extrapyramidal system consists of a number of tracts namely:

1) Vestibulo-spinal and vestibulo-bulbar tracts

There are two types of vestibulo-spinal tracts the lateral and the anterior. The lateral vestibulo-spinal tract originates from the lateral vestibular nucleus (Dieter's nucleus) in the medulla, descends in the spinal cord and terminates in the anterior horn cells of the spinal cord. This tract in addition to maintaining the vestibulo-spinal reflex also exerts an excitatory effect on the extensor anti-gravity muscles. It plays a major role in the maintenance of muscle tone and body posture. Tonic contraction of body muscles which is a vital function of the vestibular system is controlled by this tract. The vestibulo-bulbar tract has a similar effect on the extra-ocular muscles. The anterior or medial vestibulo-spinal tract originates in the medial vestibular nucleus and descends up to the upper cervical part of the spinal cord. It receives afferents from the vestibular labyrinth mainly the three semicircular canals. Its primary function is the adjustment of the head and body during angular and linear acceleration and is also concerned with manipulating conjugate horizontal eye movement and in the in the integration of eye and head movement. It, in conjunction with the tecto-spinal and tecto-bulbar tracts influences head movement in response to auditory and visual stimuli.

2) Tecto-spinal and tecto-bulber tracts

The tecto-spinal tract originates in the superior colliculus of the midbrain and terminate in the anterior horn cells of the spinal cord. Its function is the control of head movement in response to auditory and visual stimuli.

3) Olivo-spinal tract

The olivo-spinal tract originates from the inferior olivary complex and terminates in the anterior horn cells of the spinal cord in the cervical region only. Its function is the control of reflex head movements in response to proprioceptive inputs.

4) Rubro-spinal tract

The rubro-spinal tract originates in the red nucleus and descends down to the brainstem and terminates in the internuncial neurons at the base of the anterior horn cells of the upper part of the spinal cord. This tract is also involved in the maintenance of muscle tone and has a facilitatory influence on flexor muscles and an inhibitory effect on the extensor muscles.

VESTIBULAR CONNECTIONS AND PATHWAYS

Vestibulo-spinal Pathways	Vestibulo-cerebellar Pathways	Vestibulo-cerebral Pathway	Vestibulo-autonomic Pathway
Medial vestibulospinal pathway: Efferent medial vestibular nucleus fibers ➔ Descend in MLF ➔ Become medial vestibulo-pinal tract ➔ Cervical and upper thoracic motor nuclei **Function:** Stabilize Head and neck posture. **Lateral vestibulospinal pathway:** Efferent lateral vestibular nucleus fibers ➔ Descend on anterior horn of spinal cord as lateral vestibulospinal tract up to cervical region only. **Function:** Maintain the tone of the antigravity muscles of the fore-limb and thereby maintain the forelimb anti-gravity posture.	**Involved part of cerebellum:** Midline cerebellum (Archicerebellum) **Direct vestibulo-cerebellar tract:** Vestibular labyrinth ➔ Fibers directly to vermis in the midline cerebellum **Indirect vestibulo-cerebellar tract:** Vestibular labyrinth ➔ Inferior vestibular nucleus ➔ Ipsilateral inferior cerebellar peduncle ➔ Uvula and flocculonodular lobe in midline cerebellum **Midline cerebellum** ➔ Efferent fibers ➔ Bilateral vestibular nucleus complex	Efferent vestibular projections to bilateral Ventral Posterior group of thalamus. **Cortical regions of the brain known to be involved with vestibular processing:** **1. Frontal eye fields:** Control eye movements and receive vestibular motion information **2. Primary somatosensory cortex (Areas 2v and 3a):** Map body location and movement signals **3. PIVC (Parieto-Insular Vestibular Cortex):** Responds to body and head motion information **4. Posterior parietal cortex:** Motion perception and responds to both visual and vestibular motion cues **5. Hippocampus and parahippocampul regions:** spatial orientation and navigation functions	Some vestibular efferent projections to reticular formation, dorsal pontine nuclei, and nucleus of solitary tract. **Function:** Stabilize respiration and blood pressure during body motion and changes relative to gravity. The saccule senses up-down movement i.e., movement away from and towards gravity e.g., when we suddenly stand up from the sitting posture and this information has to be fed to the baroreceptors to control blood-pressure accordingly. They also have a role to play in motion sickness.

5) Reticulo-spinal tract

The reticulo-spinal tract comprises of the medial and lateral tracts that connect the reticular formation with the spinal cord. The tracts integrate information from the motor systems to coordinate automatic i.e., non-voluntary movements that are required for locomotion and for the maintenance of posture. The reticulo-spinal tract also influences the maintenance of muscle tone and mediates some autonomic functions.

6) Medial longitudinal fasciculus (MLF)

The medial longitudinal fasciculus may also be considered as a part of the extrapyramidal pathway. It has a major role in the maintenance of oculo-motor function and for the maintenance of one of the primary functions of the vestibular system i.e., gaze stabilization. The fibers of this tract originate from the vestibular nucleus, the reticular formation, the interstitial nucleus of Cajal, the posterior commissure and the superior colliculus. All these nuclei are very important for oculomotor function which is evaluated by the video nystagmography test. This tract has connections to the third, fourth, sixth, seventh, eighth and the twelfth cranial nerves. It controls the harmonious movement of the eye and neck muscles and it is due to this tract that the eyes move in the direction opposite to that of head movement but at a speed that is the same as that of the head movement. This is essential for the maintenance of gaze stabilization when the subject is moving the head. The video head impulse test (VHIT) and some other tests of vestibular function like the dynamic visual acuity test (DVA) evaluates the functional integrity of this particular function of the oculomotor system. Whenever the head moves in any particular plane, the movement is accurately sensed by the vestibular labyrinths and all details of the speed, nature, intensity and direction of the head movement is then fed to the oculomotor system. On the basis of this information, the oculomotor system generates a force to move the eyes in such a fashion that the image of the visual objects remain fixed in the fovea and any retinal slip is prevented. If the head moves from the left to the right at a speed of 200°/sec, the eyes will spontaneously move in the opposite direction i.e., from right to left at the same speed of 200°/sec. This ensures perfect gaze stabilization. The neural pathway for this passes through the medial longitudinal fasciculus (MLF).

Disorders of the extrapyramidal system jeopardize the maintenance of muscle tone and posture and also cause different types of involuntary

movement disorders like parkinsonism, chorea, athetosis, dystonia, tardive dyskinesia etc. All these disorders present with imbalance and unsteadiness in the initial stages and the clinician dealing with balance disorders should acquire the expertise of identifying each of these conditions. Most of the commonly used anti-vertigo drugs specially prochlorperazine and cinnarizine and the commonly used anti-emetic drugs induce extra-pyramidal disorders. Hence, whenever a patient presents with unsteadiness or the clinician suspects an extra-pyramidal disorder, the clinician should essentially ask whether such drugs have been used. Cinnarizine and flunarizine are very commonly prescribed by doctors for prolonged periods and quite often patients also purchase these drugs over the counter. But both these drugs are known to induce Parkinsonism. In fact cinnarizine is the commonest cause of drug-induced Parkinsonism.

Summary

When discussing the physiology of maintenance of balance we are actually dealing with a very complex system and on a very wide canvas where (1) the skeletal muscles of the body and the extra-ocular muscles of the eyes are involved, (2) the ears are involved, (3) the proprioceptors on the feet/ buttocks/ back and that of the neck are involved, (4) the spinal cord and the different neural pathways in the brain, spinal cord and peripheral nerves are involved and over and above these, (5) the cognitive system, (6) the cerebellum, (7) the neural system, and (8) the different neural pathways are involved. It is now known that even (9) the limbic system and the (10) hippocampus are involved. This is a huge platform involving multiple systems and organs of the body viz., the musculoskeletal system, the central and peripheral nervous system, the visual system, the vestibular system and the cognitive and even the psychic system. The balance system is the only system in the body where so many different and diverse systems are involved. This is what makes the anatomy and physiology of the balance system so very complex.

To treat a patient of vertigo ethically and logically and to comprehend the underlying pathology that is causing the balance disorder, the clinician must acquire a very clear grasp of the convoluted anatomy of the balance system and also understand the complex clinical physiology in health and disease especially the aberrations in function when the balance system is partly or wholly deranged by disease.

3 'Must Knows' of Physiology of the Balance System

What constitutes the balance system:	Balance function in normals:	Aberrations in the functioning of the balance system:
the convoluted ANATOMY of the vestibular system	*the complex PHYSIOLOGY*	*when the balance system is deranged*

The Reflex Pathway for Maintenance of Balance

As previously discussed the maintenance of balance is a reflex phenomenon. The dictionary defines a reflex as an action or movement not controlled by conscious thought. A reflex is a rapid, involuntary response to a stimulus ***(Fig 8 A)***. A reflex arc is the neural pathway traversed by the nerve impulses from the part which is stimulated to generate the reflex to the part where the involuntary response is generated i.e., where the reflex response happens. All reflexes have a reflex arc that consists of:

- ***an afferent sensory organ*** which needs to be stimulated to generate the reflex;
- ***an afferent neural pathway*** that carries the neural impulse generated at the afferent sensory organ to the center of the reflex arc,
- ***the center of the reflex*** where the neural signal is generated,
- ***an efferent neural pathway*** that carries the neural signal generated in the center of the reflex to the effector motor organ, and
- ***an effector motor organ*** where the final response takes place.

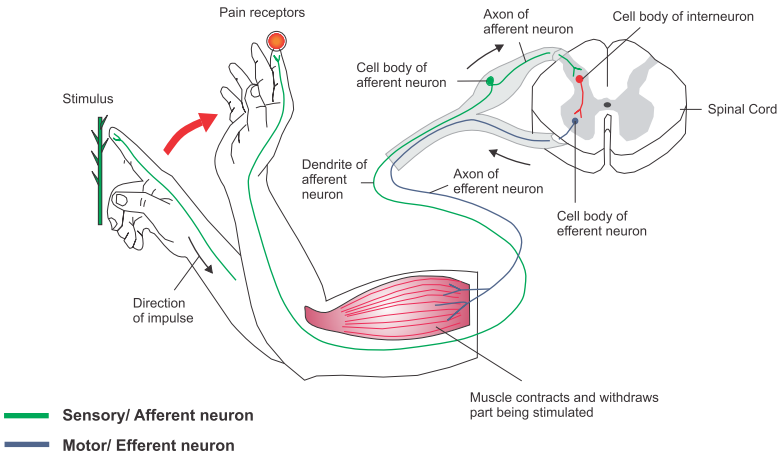


Fig 8 A. The Reflex Arc.

Examples of a reflex are:

a) A hiccup to the involuntary response of irritation to upper Gastrointestinal system. Afferent signals are transmitted via the phrenic nerve to the effector organ which is the diaphragm.

b) Another such example is *the response that occurs in the knee-jerk reflex.*

The eyes, the proprioceptors and the vestibular labyrinths in the ears are stimulated whenever there is any movement of the ground and/ or the surroundings or of the head/ body. The involuntary response to this stimulation is the requisite contraction of specified muscles of the eyes as well as that of the body such that the functions of the balance system i.e., maintenance of gaze stabilization and maintenance of perfect erect posture are very precisely served.

The vestibular labyrinth in the ear which is the afferent sensory organ for the reflex arc of the vestibular system collects the information about the stability of the head/ body and passes this information in the form of neural codes or action potentials through the vestibular nerve (8th cranial nerve) which in this case is the afferent neural pathway and reaches the center of the reflex which is the vestibular nucleus; from the vestibular nucleus the neural impulse passes through the efferent neural pathway (also termed as the efferent motor pathway) which is the medial longitudinal fasciculus (MLF) and the descending tracts of the spinal cord to the motor nuclei of the eye muscles (nuclei of the 3rd, 4th, 6th cranial nerves) and from there to the extra-ocular muscles of the eyes to move the eyes and to the anterior horn cells of the spinal cord and from there to the muscles of the limbs and trunk to move the body muscles ***(Fig 8 B)***.

The neural pathway from the vestibular nucleus in the brainstem to the muscles of the eyes and body is the efferent neural pathway and the muscles of the eyes and that of the limbs and trunk are the effector motor organs. In response to the stimulus received in the vestibular labyrinth, the muscles of the eyes and the body will contract reflexly in a very specified and precise way to maintain gaze stabilization and postural stabilization which are two major functions of the body's balance system. This is how the entire system works. If any one part of this reflex arc is defective or is performing subnormally, the entire body's balance system gets jeopardized and the subject feels vertiginous and/ or has a feeling of unsteadiness.

The Reflex Pathway

AFFERENT SENSORY ORGAON
Vestibular labyrinth/Eyes/Proprioreceptos

AFFERENT NEURAL PATHWAY
Vestibular nerve/ Optic nerve/ Ascending column in spinal cord

CENTRE OF THE REFLEX
Vestibular nucleus

EFFERENT MOTOR PATHWAY
MLF to oculomotor nuclei 3/4/6 cr nv
Descending vestibulospinal tract
Anterior horn cells - peripheral

EFFECTOR MOTOR ORGAN
Extra-ocular/ skeletal muscles

Fig 8 B.

The Reflex Pathway:

Here only the ***afferent pathway from the vestibular labyrinth is shown.*** Similar pathways are there from the proprioceptors and from the eyes which are the two other afferent sensory organs of the reflex arc of the balance system just like the vestibular labyrinths; the sensory nerves from the proprioceptors are the neural pathways that carry vibratory sense through the ascending columns in the spinal cord and are the afferent neural pathways for the proprioceptors. The optic nerve is the afferent sensory pathway from the eyes. The efferent pathway of the reflex arc for the proprioceptors and of the eyes is the same as that described for the vestibular labyrinths i.e., the descending column in the spinal cord ➔ anterior horn cells ➔ peripheral nerves for the body (skeletal) muscles that carry out the contraction of muscles of the limbs and the trunk and the 3rd/ 4th and 6th cranial nerves which are the efferent motor pathways for the eye movement.

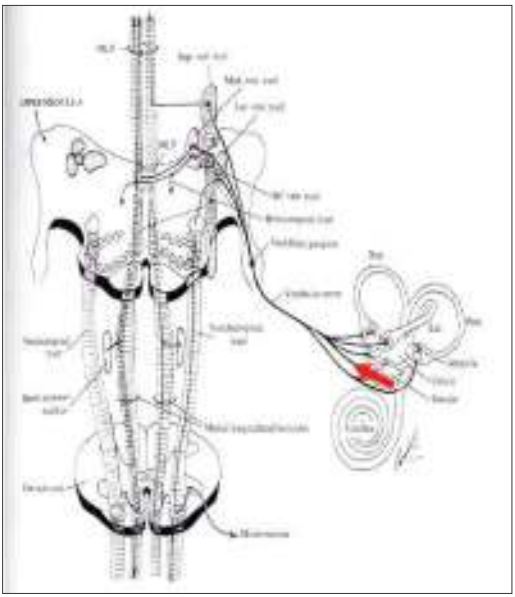
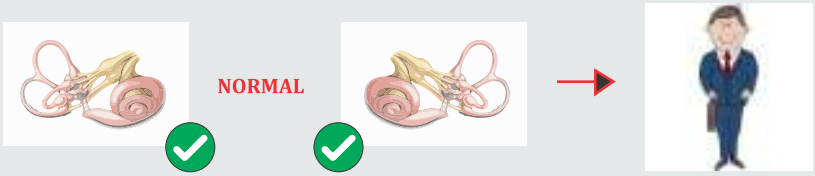


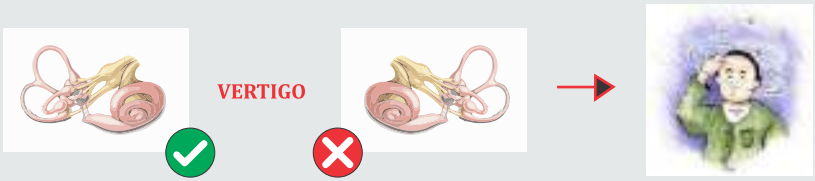
Fig 8 C.

MAINTENANCE OF BALANCE

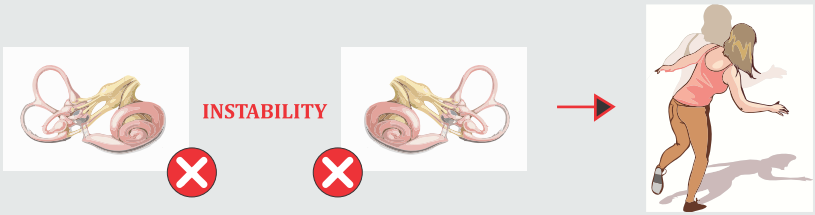
RIGHT Labyrinth		LEFT Labyrinth	



When **both labyrinths are working NORMALLY,** the balance is maintained and the subject is standing perfectly erect.



When there is damage of one labyrinth the subject gets a spinning sensation which is caused by the **DISPARITY** in the electrical impulses of the two sides. The condition is shown when there is a defect in the left labyrinth. The left sided unilateral vestibulopathy will generate a right beating nystagmus.



When both labyrinths are damaged together there is a sensation of imbalance or **UNSTEADINESS.** There is not much of any spinning sensation as now there is NO disparity between the labyrinths of the two sides.

Vestibular Labyrinth and its Different Functions and Connections

Overview

The vestibular labyrinth senses head and body movement. It has five different sensors for this purpose; ***the three semicircular canals and the two otolith organs viz. the utricle and the saccule (Fig 10).*** Each part of the vestibular labyrinth monitors one particular type of movement. Linear and/ or translational movement is sensed by the otolith organs i.e., the saccule and the utricle and angular movement is sensed by the semicircular canals.

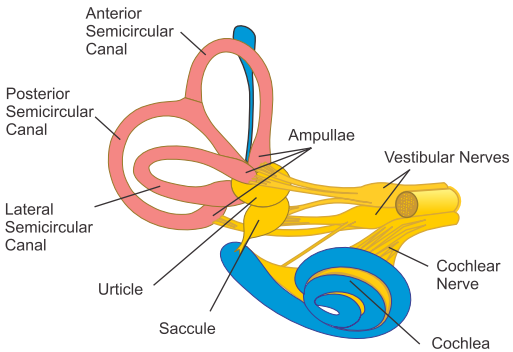


Fig 9. The Vestibular Labyrinth.

When we turn the head from left to right or right to left or when we move the head at the neck from up to down or down to up it is an angular or ***rotational movement***; which is sensed by the semi-circular canals but when we are going up or down in a lift or standing on a moving platform or are moving forward or backwards on plain ground then it is a ***translational or linear movement*** and that is sensed by the otolith organs.

Up-Down movement is monitored by the ***saccule***, ***Forward-Backward and side to side movements*** are monitored by the ***utricle***. The three ***semicircular canals*** monitor the ***angular movement*** in different directions.

The three semicircular canals are oriented in three different planes which are perpendicular to each other. In whatever angle we move the head, two of the six semi-circular canals (three on each side) will be stimulated and movement in any angle will be accurately sensed. Any movement of the head or body will be sensed by the vestibular sensors and will spontaneously (i.e, reflexely) elicit requisite corrective movement of the eyes and/ or the body muscles to maintain gaze stability and postural stability which are two of the three major functions of the vestibular system. The corrective eye/ body movement is effected by contraction of specified muscles in the eyes and that of the limbs and trunk as already explained. This is explained in a little more details below. The mechanism is somewhat complex and does not justify complete and elaborated explanation in a treatise for practicing clinicians.

Functions & Connections of Vestibular Labyrinth in Maintenance of Balance

Within each semicircular canal there is a special sensory epithelium – ***the ampulla*** which gets stimulated whenever the head suddenly moves and remains stimulated till the speed of head movement attains a fixed speed. This happens as the semicircular canals are sensitive to acceleration only which is the measurement of change of speed (either or decrease of speed). When there's no change of speed and the head is rotating at a fixed speed then the semicircular canals are not stimulated. The semicircular canals open at both ends into the utricle. The semicircular canal contains a liquid called ***endolymph*** which is displaced during rotational movements of the head because of its inertia. The ampulla is an enlargement or swelling at one end of each semicircular canal ***(Fig 10)***. Contained within the ampulla is the ***cupula,*** which is a gelatinous mass, attached to hair cells.

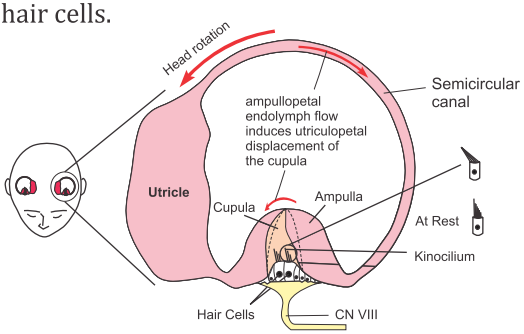


Fig 10. The lateral semicircular canal of left side showing ampulla and cupula, and the displacement of endolymph within semicircular canal which deflects the cupula. Head turning towards the left side causing emdolymph movement towards the ampulla of the left lateral canal.

The cupula is a pliable structure that seals the inner diameter of the semicircular canal at the ampulla as shown in figure 11. In the cupula there are hair cells which are like the hair cells of the cochlea and function more or less in the same way. The hairs of the hair cells in the cupula are arranged in a set pattern from large to small (tallest to shortest) as shown in the adjoining figures. The longest/ tallest hair cell at one end is called the kinicillium and the others are called sterocillia. Movement of the endolymph in the semicircular canals bends the hairs jutting out from the hair cells. When there is no movement of the head, the hairs of the hair cells are straight but the hair cells are not sitting idle; they constantly keep on discharging action potentials (spikes) with a firing rate of about 80 to 100 spikes per second which is called the resting potential of the hair cells. But when the head moves in any direction there is bending of the hairs of the

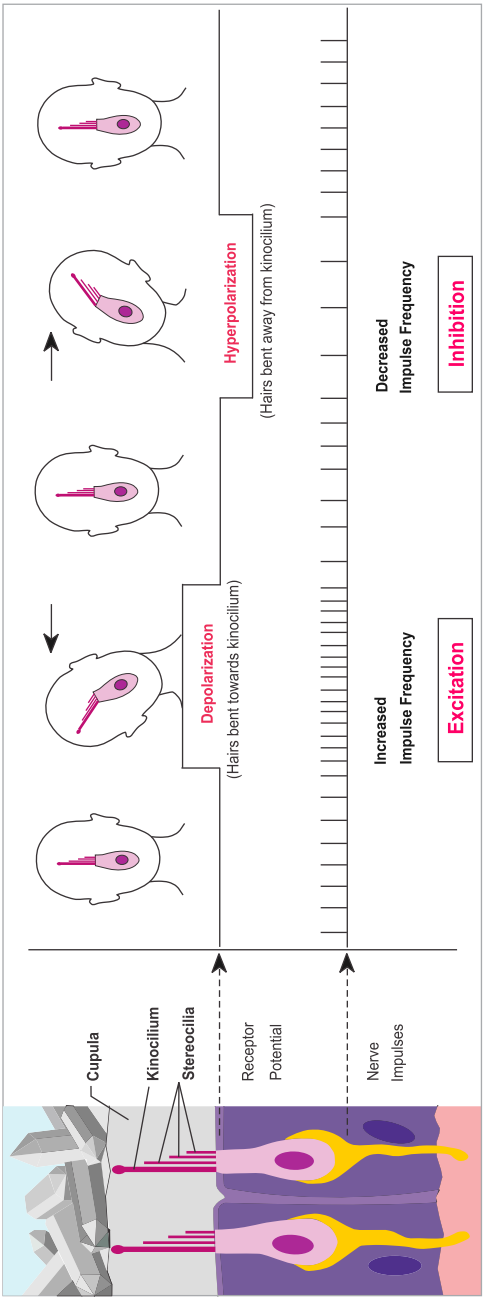


Fig 11: Morphological disposition and physiological polarization of the hair cell bundles in the cupula of the semicircular canals causing Excitation and Inhibition.

hair cells as the endolymph is displaced within the semicircular canal. Bending of the hairs in a particular direction opens the filament (shown in the adjoining figure) between the hairs of each haircell. When the filament opens, the endolymph (which is high in K+ and low in Na+) that surrounds the hairs of the hair cells can enter the hair cells. The endolymph has a +80 mv charge with respect to the hair cell which is negatively charged. The endolymph's positive voltage pushes K+ into the negatively charged hair cell. When this happens, the hair cell depolarizes, releasing neurotransmitter. This causes an increase in the frequency of generation of action potentials (AP) in the vestibular nerve afferent fibers that originate from the hair cells.

This increase of action potential caused by bending of the hair cells towards the kinocillium is called depolarization or excitation of the cells. The opposite of depolarization/ excitation is called hyperpolarization or inhibition. Hyperpolarization or inhibition occurs when the projecting hairs of the hair cells are moved away from the kinocillium. Depending on the direction of movement of the endolymph in the semicircular canal there will be either depolarization or hyperpolarization in the particular semicircular canal.

When the head moves to the right in the standing/ sitting position, the endolymph in the right lateral semicircular canal due to its inertia causes a relative movement (or displacement) of the endolymph towards the ampulla (i.e., towards the left side) in the direction which is opposite to that of the head movement. The orientation of the hairs of the hair cells in the cupula of the right lateral semicircular canal is such that when the endolymph in the right lateral semicircular canal is moving towards the ampulla, then the hairs bend towards the kinocillium. This causes a depolarisation or excitation of the right lateral semicircular canal. The opposite thing happens in the left lateral semicircular canal during this rightward movement of the head. When the head is moving to the right, the endolymph moves in the opposite direction (i.e., in the same direction as that of the head movement) in the left lateral semicircular canal due to the inertia of the endolymph in the left lateral semicircular canal. Hence in the left lateral semicircular canal the movement of the hairs will be away from the kinocillium which results in hyperpolarization or inhibition of the left semicircular canal. So in a rightward head movement i.e., when the head is turned to the right, there will be excitation of the right lateral semicircular canal and inhibition of the left lateral semicircular canal.

Any movement or displacement of the endolymph within a semicircular canal deflects the cupula. Movement of endolymph towards the ampulla is called ampullopetal movement and the movement of endolymph away from the ampulla is called ampulofugal movement. J R Ewald, a German physiologist had pronounced three laws on the functional behaviour of the semicircular canals. Ewald's laws are as follows:

1) ***Ewald's first law*** states that stimulation of the semicircular canal causes a movement of the eyes in the plane of the stimulated canal; this means that if the lateral (horizontal) canals are stimulated there will be movement of the eyes in the horizontal plane (horizontal nystagmus- either left beating or right beating depending upon which canal is stimulated) as the lateral canals are positioned in the horizontal plane, and if the anterior or posterior canals (which are vertically dispositioned) are stimulated there will be eye movement in the vertical axis.

2) ***The second law*** states that in the lateral semicircular canals, ampullopetal movement of endolymph causes a greater stimulation than an ampullofugal movement of endolymph. The implication of Ewald's second law is that the magnitude of excitation of a semicircular canal can be more than the magnitude of inhibition of the complementary (or partner) canal. This happens because when a semicircular canal is stimulated depending upon the speed of stimulation of the canal the excitation can go up to infinity spikes per second but the inhibition cannot be less than zero spikes per second.

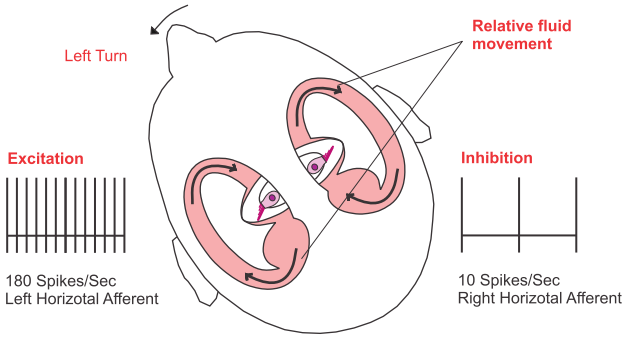
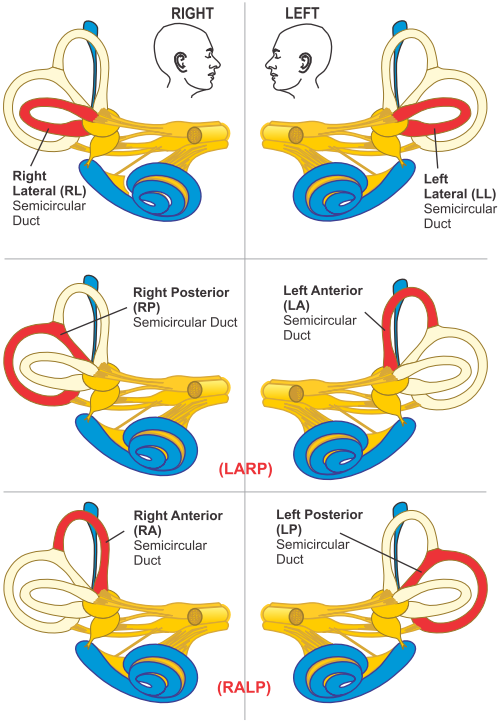


Fig 12. Relative fluid movement in the semicircular canals and generation of excitatory and inhibitory response.

Usually at normal speeds of head movement during our day to day activities the excitation of the hair cells can rise from the resting potential of say 100 spikes/ second to about 400 spikes /second but the inhibition

in the complementary (or partner - explained below ***Fig 13***) semicircular canal can go down to a minimum of zero spikes per second. It cannot go down below that. Hence, if the left lateral semicircular canal is completely damaged but the right lateral semicircular canal is functioning normally, then the right semicircular canal will generate a higher rate of action potentials when the head is turned to the right side (due to ampullopetal flow of endolymph in the right lateral semicircular canal) but much less action potentials when the head is turned to the left side (ampullfugal flow of endolymph in the right lateral semicircular canal). This is the basis of the now very popular clinical head impulse test and the new vestibular investigation called video head impulse test (VHIT). For a more detailed explanation the interested reader is referred to the chapter on Video Head Impulse Test in CLINICAL AUDIO-VESTIBULOMETRY for Otologists and Neurologists 5th edition – Dr Anirban Biswas - published by Bhalani Medical Book House Mumbai, India).



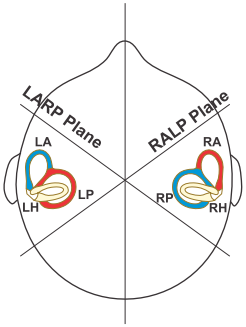


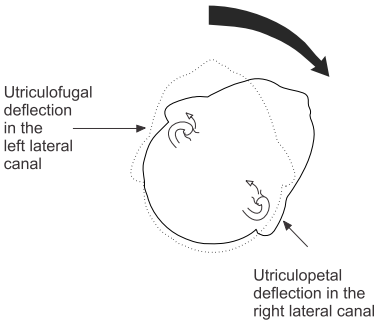
Fig 13. Complimentary sets of the semicircular canals and the push-pull mechanism.

3) Ewald's third law states that in the anterior and posterior semicircular canals ampullofugal flow of endolymph causes excitation and hence greater stimulation, then ampullopetal flow of endolymph which causes inhibition and hence lesser magnitude of generation of action potentials. As explained previously excitation will always be unlimited and it can go or up from the resting potential of 100 spikes/ second to any level (even 400 or more spikes/ second, but inhibition cannot go down below 0 spikes/ second.

Another important law related to eye movements and nystagmus is Alexander's Law. It states that the intensity of a jerk nystagmus increases when the subject looks in the direction of the fast phase. This dictum is definitely true for a peripheral vestibular nystagmus but not always for a central nystagmus. If the intensity of a nystagmus increases when the subject looks to the direction of the slow phase (i.e., if the subject having a right beating nystagmus looks towards the left side) then it is indicative of a central lesion.

Two semicircular canals, one from each side form a complimentary (or partner) set. The two lateral canals (i.e., the left and the right lateral canals) are one set, the right anterior and left posterior together are the second set and the left anterior and right posterior together are the third set. For any head movement one canal of each set is stimulated and the other canal of the same set is inhibited; hence if the right lateral canal is stimulated, then the left lateral canal is inhibited. The excitatory and inhibitory activity in each of the three sets of complimentary canals works as a push-pull mechanism and augments the neural response ***(Fig 13).***

This means that if due to a head movement in the horizontal plane, there is an excitatory response of (say) +2 generated in the right lateral canal then a -2 response is automatically generated in the left lateral semicircular canal due to the peculiar disposition of the two semicircular canals of each complimentary set. This happens because when there is head movement in one direction and if there is an



ampullopetal deflection of the cupula in the right lateral canal (causing excitatory response) there is also a simultaneous ampullofugal deflection of the cupula in the left lateral canal generating an inhibitory response. The magnitude of the impulse fed to the vestibular system from such a movement is the sum of the excitatory and inhibitory response which is 2+2=4 and not +2-2=0. Both excitatory and inhibitory signals are sent from the ampulla of the semicircular canals through the vestibular nerve to the four vestibular nuclei namely medial vestibular nucleus, lateral vestibular nucleus, inferior vestibular nucleus and superior vestibular nucleus.

Vestibulo-Ocular Reflex

The information on head turning generated in the semicircular canals traverses in the form of neural impulses (or stimuli) from the vestibular nucleus through the medial longitudinal fasciculus to the oculomotor centers and finally generates a precise contraction of the extra-ocular muscles. This contraction brings about the corrective eye movement for gaze stabilization. While traversing the neural pathway it undergoes some neural processing influenced by the inputs from the cerebellum and other parts of the brain such that the eye movement generated on the basis of the information about head movement obtained from the semi-circular canals is very precise and perfectly tuned.

Excitation of superior or anterior semicircular canals causes contraction of the ipsilateral superior rectus and contralateral inferior oblique muscles as well as the relaxation of the ipsilateral inferior rectus and contralateral superior oblique muscles, while excitation of posterior semicircular canals cause contraction of the ipsilateral superior oblique and contra-lateral inferior rectus muscles and relaxation of the ipsilateral inferior oblique and contralateral superior rectus muscles. Contraction of the ipsilateral medial rectus and contralateral lateral rectus muscles and relaxation of the contralateral medial rectus and ipsilateral lateral rectus muscles occurs due to excitation of the lateral canal. Horizontal eye movement towards the side opposite to that of the head movement occurs due to this ***(Fig 14).*** Movement of the head to the left will stimulate the left lateral semicircular canal. Stimulation of the left lateral semicircular canal will cause contraction of the left medial rectus and right (i.e., contralateral) lateral rectus and relaxation of the right medial rectus and

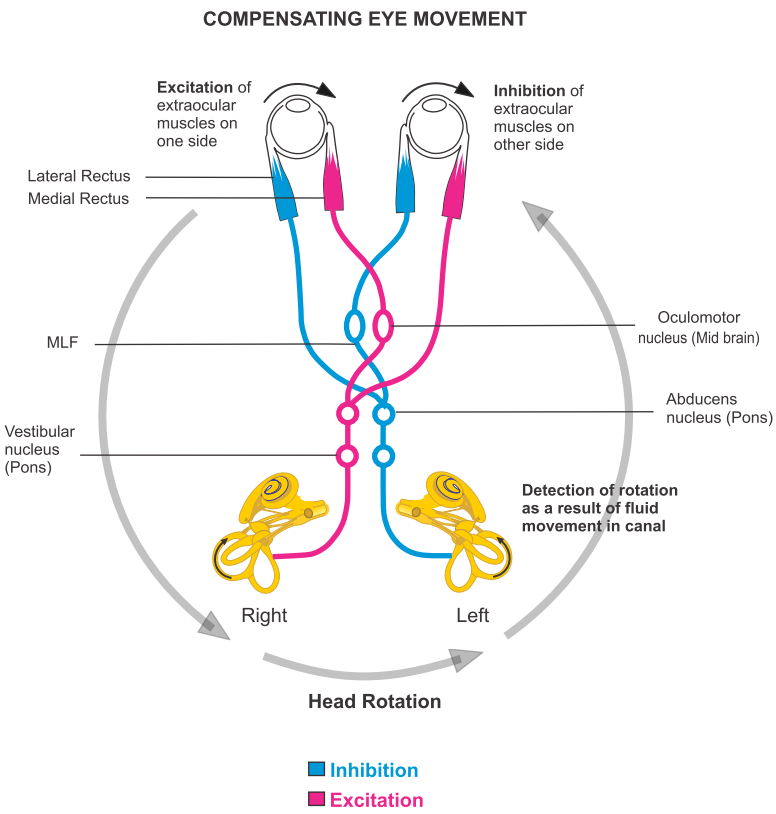
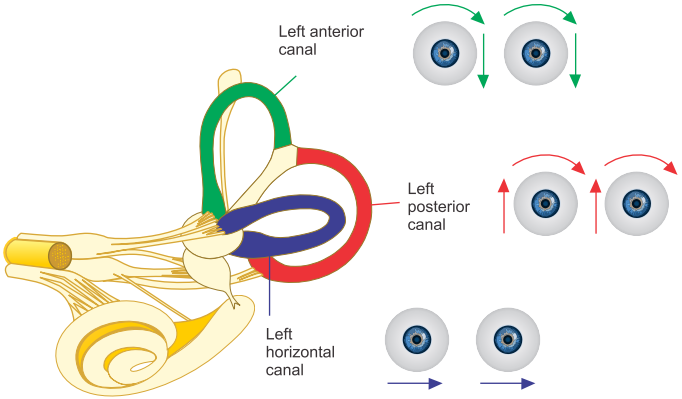


Fig 14. Vestibulo-ocular Reflex (VOR)

When the head moves from left to right in the horizontal axis, the right lateral semicircular canal hair cells depolarize (increase of action potentials) while those of the left lateral semicircular canal hyperpolarize (decrease of action potentials). The outcome of this is that the vestibular afferent activity of the right side increases and that of the left side decreases. As this activity is relayed to the vestibular nuclei through the vestibular nerve, the neural activity of the right vestibular nuclei increases while that in the left vestibular nuclei decreases. When this happens, motor neurons in the left 6th and right 3rd cranial nerve nuclei fire at a higher frequency while those in the left 3rd and right 6th cranial nerve nuclei fire at a lower frequency. The result of this is that the left lateral rectus and the right medial rectus contract whereas the left medial rectus and the right lateral rectus relax. This makes both the eyes rotate leftward. Hence when there is a rightward head movement there is a corresponding leftward eye movement. This is the basis of the vestibulo-ocular reflex to keep images fixed in the fovea (process of gaze stabilization).

left (i.e, ipsilateral) lateral rectus muscle. The result of this is a movement of the eyes laterally to the right i.e., to the side opposite to that of the head movement.



Linear or translational movements stimulate the otolith organs. In both the otolith organs there is a special sensory epithelium – the macula which is functionally just like the ampulla of the semicircular canals and gets stimulated whenever the head suddenly moves in the linear axis or the body undergoes a translational movement. Stimulation of the utricle and saccule also causes movement of the eyes by contraction and

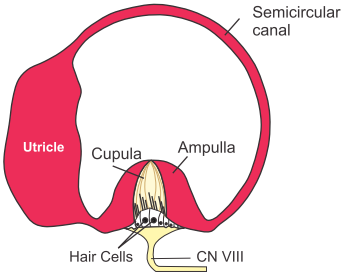
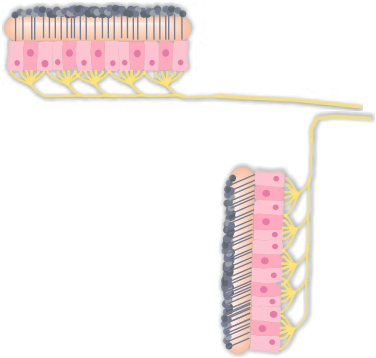


Fig 15. Ampulla and cupula.



Summary

All these five sensors of each vestibular labyrinth sense completely different types of head/ body movements. So if one of these five sensors is defective, one particular type of movement will not be sensed. If a movement is not sensed, the brain is deprived of the information on that particular movement type and so the vestibular system will not generate the corrective eye/ body movement. This will result in deranged gaze stabilization and deranged postural stabilization due to which the subject will feel giddy and unsteady. Many if not most head and body movements are a combination of angular and linear movements and involve stimulation of the semicircular canals as well as the otolith organs.

Tests to ascertain the functional status of the sensors have to be carried out on all of the five sensors separately, the three semicircular canals, as well as the saccule and the utricle of each side individually. The caloric test evaluates only the lateral semicircular canal. It does not test the utricle, saccule, anterior canal or the posterior semicircular canal. By performing the caloric test the clinician will have absolutely no idea on how the balance system is behaving because it tests only one of the five sensors. This is extremely relevant in clinical practice. Modern vestibulometry allows us the facility to evaluate the structural and functional integrity of each of the five different sensors of the vestibular labyrinth of each side with utmost precision. Vestibulometry of today not only offers us the facility to evaluate the functional status of each of the vestibular sensors individually but also at different frequencies of stimulation. So evaluating the physiology or the bio-mechanism of the functioning of the vestibular labyrinth very comprehensively and completely is possible and is a must today in all balance disorder patients.

FUNCTIONS Of Balance System

- **Gaze Stabilization (by VOR)**
- **Postural Stabilization (by VSR)**
- **Correct Perception of Verticality (by Otolith Organs)**

Gaze Stabilization

The nuances of Gaze Stabilization

The goal of gaze stabilization is to maintain a stable & clear image of the visual surroundings when:
1) head is moving but visual target is stable,
2) head is stable but visual surroundings/ target is stable,
3) both head & visual surroundings/ target are moving.

This is primarily carried out by the vestibulo-ocular reflex (VOR) but other mechanisms like the oculomotor system and the cerebellar systems that work in conjunction and modulate the VOR are also involved in the execution of the reflex. The VOR involves the execution of a conjugate eye movement that moves the eyes very fast and spontaneously in a direction opposite to the direction of head movement. The eye movement is at a speed of about 800 degrees/ sec and has a reaction time of about 15 millisecs only. The VOR is cancelled or suppressed in normal persons when there is a visual target that is moving in the same speed and same direction of the head movement. This suppression of VOR is a CNS mechanism and failure of VOR suppression is indicative of a CNS abnormality - a mechanism that needs to be tested in balance disorder patients, it is called the Vestibulo-Ocular Reflex Suppression (VORS) test.

Supranuclear Oculomotor System

Though the vestibulo-ocular pathway which is the connection between the vestibular nuclei and the motor nucleus of the 3rd, 4th and 6th cranial nerves is hyped as the main neural pathway for gaze stabilization, yet there are other supra-nuclear connections (higher CNS centers that control the activity of the motor nuclei of the 3rd/ 4th/ 6th cranial nerves) of the vestibular nuclei which are no less important. These neural connections carry out different functions related to gaze stabilization in different challenging situations.

Gaze stabilization is not always as simple as the example discussed previously that is looking at a stationary car and suddenly moving the head whereby the eyes move spontaneously in the opposite direction at the same speed as the head movement to maintain gaze stabilization.

Gaze stabilization is a very complex biological mechanism as the visual system is exposed to various types of complex visual conditions where gaze stabilization is very challenging and just the simple vestibulo-ocular reflex (VOR) as described above is not adequate to stabilize gaze. The oculomotor system of the central nervous system then works in conjunction with the VOR to stabilize gaze. The oculomotor system is the motor system to move the eyes in complex and challenging visual situations so as to fixate/ stabilize images of surrounding objects in the fovea and there by provide good visual acuity and spatial orientation in challenging visual conditions. It is a very complex process & involves many mechanisms controlled by supra-nuclear centers. These supraneuclear centers are all a part of the central nervous system. Functionally, they execute the oculomotor mechanism of gaze stabilization and are structurally connected to the eyes and the vestibular labyrinths.

Supranuclear OCULOMOTOR centers in the brain

Important Supranuclear OCULOMOTOR centers in the brain are:

rMLF: Rostral interstitial nucleus of medical longitudinal fasciculus (upper midbrain)

INC: Interstitial nucleus of Cajal (upper midbrain)

PPRF: Paramedian Pontine Reticular Formation

NPH: Nuleus Praepositus Hypoglossi

PC: Posterior Commissure (connects the rMLF of 2 sides)

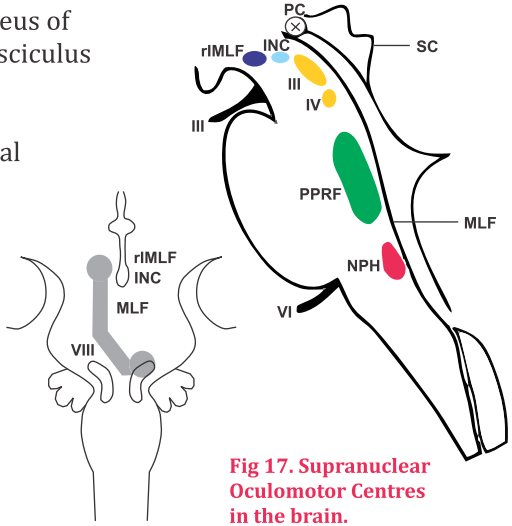


Fig 17. Supranuclear Oculomotor Centres in the brain.

When the function of any of these supra-nuclear oculomotor centers are jeopardized, gaze stabilization is disrupted and leads to CENTRAL VERTIGO; hence a very thorough evaluation of oculomotor system is mandatory in all patients presenting with balance disorders. Different clinical tests and where possible the oculomotor tests of VNG/ VHIT are performed to evaluate the functional status of the oculomotor system. These tests are described in details in the Clinical Audiovestibulometry 5th edition, published by Bhalani Medical Book House, Mumbai, India. (http://clinicalaudiovestibulometry.com/) but are briefly covered here.

Supranuclear Oculomotor Mechanisms

1) Smooth pursuit system
2) Saccadic system
3) Convergence system
4) Visual fixation with gaze holding system
5) VOR and suppression of VOR by visual fixation
6) Optokinetic system

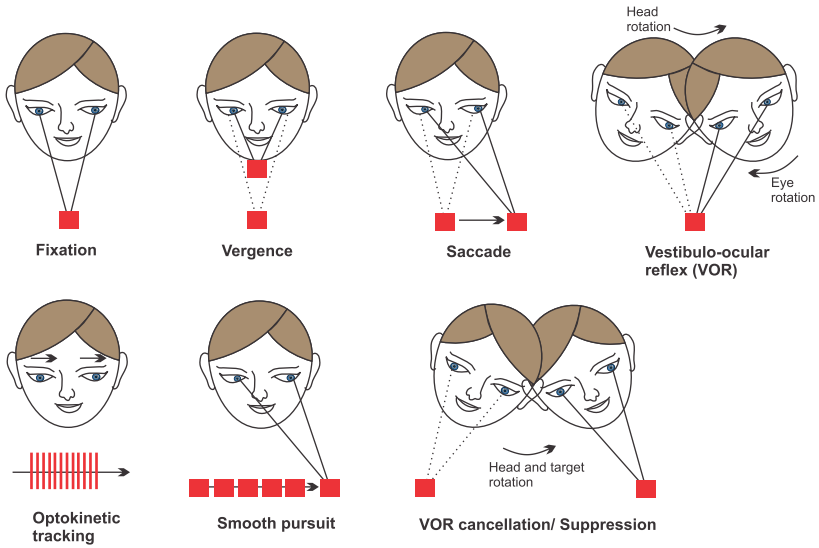


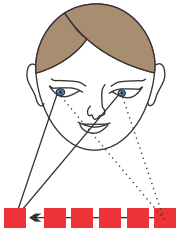
Fig 18. Gaze Stabilization: Supranuclear Oculomotor Mechanisms.

1) Smooth pursuit/ tracking system (SPS)

Smooth pursuit/ tracking system (SPS) allows the eyes to closely follow a moving object very often against a fixed visual backdrop but even when there is no backdrop. Suppose I am looking at the sky and my eyes are fixed at one of the clouds and the image of the cloud is there in my fovea. Suddenly a bird appears on one end of the visual field and traverses the entire visual field from one end to the other end. So the eyes will have to keep the image of the cloud in the fovea, as well as track the moving bird at the same time - the image of which will also have to be continuously fixed in the fovea in spite of the bird moving.

Functions: In a situation like this, the smooth tracking system, which is a part of the oculomotor system, will help the vestibulo-ocular reflex to keep the image of the sky stationary as well as fixate the image of the moving bird in the fovea. This is an example of a smooth tracking system. When we are looking at a moving pendulum or looking at a flying airplane or a bird flying in the sky or looking at a model walking the stage side to side we are using the smooth tracking system to fixate the image of the moving object in the fovea.

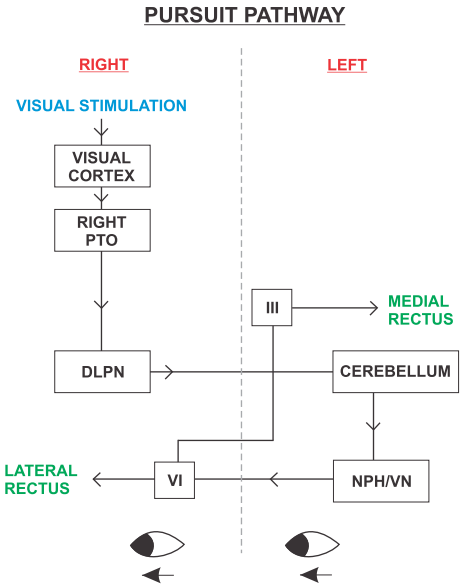
The smooth tracking system functions only when the eyes track a moving object that is traversing a predictable trajectory and is moving at a speed of less than 1.2Hz. The smooth pursuit system works best under this condition only and fails if the speed is more than 1.2Hz or the trajectory is uneven i.e., if the moving object abruptly changes speed or follows an unpredictable and changing trajectory.



Smooth pursuit

PURSUIT SYSTEM:

Control of smooth pursuit eye movements is a complex process. The stimulus for pursuit movement is movement of an image across the fovea at velocities greater than 3 to 5 degrees per second. Visual (striate and peristriate) cortex projects to parieto-temporo-occipital junction (PTO) as well as to Frontal eye field (FEF). The PTO projects via the internal saggital striatum and the posterior limb of internal capsule to ipsilateral dorsolateral and lateral pontine nuclei(DLPN). Pursuit pathways control ipsilateral tracking hence undergo double decussation.



CNS involvement: The vestibulo-cerebellum (flocculus, nodulus, and posterior vermis) plays a dominant role in smooth pursuit; the remainder of the cerebellum, portions of the brain stem, and cortical areas also participate ***(Fig 19).*** Defects in smooth tracking may be due to disorders in the Visual cortex, Extra-pyramidal system, the Dorso-lateral pontine nuclei, the cerebellum and also in the Oculo-motor nuclei.

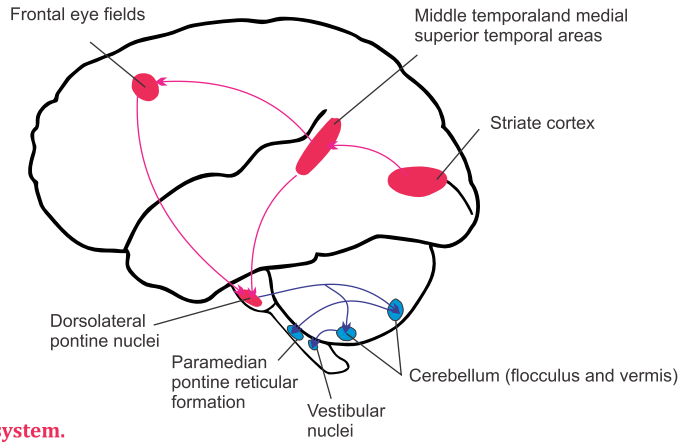


Fig 19.
CNS involvement in Smooth pursuit system.

In diseases of the cerebellum/ brainstem and in some cortical disorders the smooth pursuit becomes erratic and irregular leading to defective visual stabilization of smoothly moving objects. Hence SPS defects do not allow topographical/ etiological diagnosis but indicates that there is a disorder in the oculomotor/ central vestibular system.

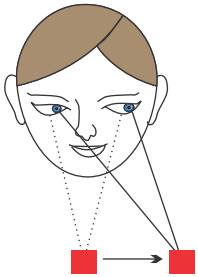
Testing: In the clinic we can test the smooth tracking system by the smooth pursuit test. The clinician asks the patient to look at raised index finger and moves the finger side to side; as the clinician moves his fingers he is looking at the patient's eyes to see whether it is moving smoothly and sinusoidally or not. If the eyes are not moving smoothly and the eye movement is jerky then a problem in the Smooth tracking system is suspected. While performing the VNG/ ENG test or the VHIT we test the smooth tracking system by the Pendulum Tracking Test. If SPS is defective, gain is too low to keep image of a smoothly moving target in the fovea and eyes compensate this by corrective saccades, hence saccades are obtained in smooth tracking. Saccades are jerky eye movements whereas the smooth pursuit/ tracking movements are perfectly smooth, non-jerky movements. Hence if the eyes move with jerks or with pauses or jumps from one point to another a defect in this smooth tracking system is evident.

Fig 20. Pendulum Tracking Test for evaluation of smooth pursuit system

2) The saccade system

The saccade system is for stabilizing image of a visual target at the end of the visual field in the fovea by a rapid single eye movement. It facilitates visual tracking when SPS fails and when speeds are more than 1 Hz (rather 1.2Hz). The primary functional goal of the saccadic movements is to reposition a visual target of interest onto the fovea with a single rapid eye motion.

CNS involvement: To accomplish this task, supratentorial processes (cortex/ cerebellum/ basal ganglia/ etc.) must participate to calculate the strength of the neural signal to be delivered to the extra-ocular musculature needed to stimulate a rapid and accurate single movement of the eyes. In addition to the cortical activity, the pontine reticular formation and the vestibulo-cerebellum participate in modulating the parameters of movement, such as the velocity of the saccade, its latency of onset, and the accuracy of the saccade. When a target of interest is moving outside the operating parameters of the smooth pursuit system, the saccade system facilitates the tracking ability by superimposing jerk movements onto the smooth movements. A saccade is a quick, simultaneous movement of both eyes between two or more spots of fixation. An example will clarify this.


Saccade

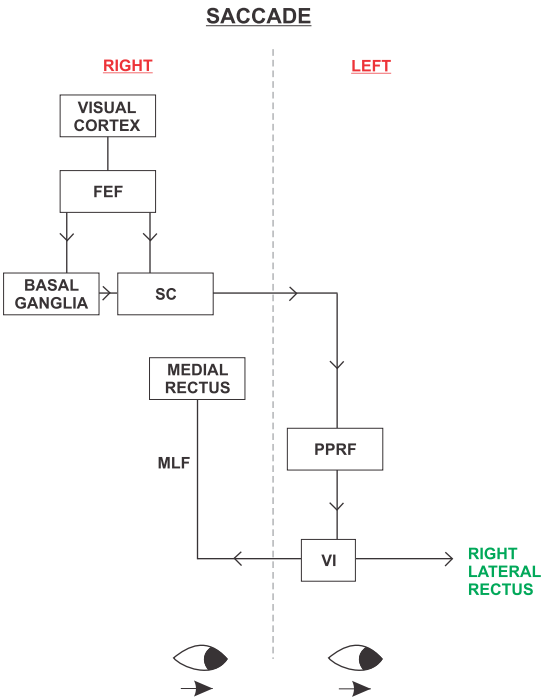
Supposing the subject is looking at an object of interest in front of him in the center of a large room, suddenly another person (say) a guest enters the room from a side door. Now the subject has to keep the image of the guest coming from the side door in the subject's fovea also. Immediately there will be shifting of the eyes that will fixate that image of the new object/ target of interest i.e., the guest in this example at the far end of the visual field. In a situation like this when the subject has to fixate vision very fast and bring images of visual targets into the fovea by very fast and very precise eye movements it is the saccadic system that executes the function of gaze stabilization.

Functions: Saccadic system's function is to suddenly move the eyes and fix it over the visual object of interest not only at the end of the visual field but at any point of the visual field. However the function of the saccadic system is not to keep the eyes fixed over there and its function finishes immediately after taking the eyes to the new object of interest.

Now supposing in the example above, the guest who has entered the room from the side door and comes in front of the subject, the smooth tracking system will track the guest coming from the side door to the center. But, supposing the guest does not enter the room to allow the smooth tracking system to track the guest and keeps standing at the door, it will be another oculomotor system called Gaze holding system that will fixate the gaze and keep the image of the guest standing in the side fixed of the visual field in the fovea.

SACCADE:

Stimulation of FEF by visual stimuli generate saccade which shifts eyes to opposite side i.e. stimulation of right frontal eye field left oriented saccade. Signals from FEF are relayed via three pathways, one is direct pathway from FEF to PPRF on opposite side, second via Superior colliculus and third via basal ganglia.



PPRF contains excitatory burst neurons (EBN) which fire just at the onset of saccade. These EBN are tonically suppressed by omnipause neurons present in nucleus raphe interpositus rostral to abducent nucleus. When these omnipause neurons receive input from cerebrum, cerebellum and superior colliculus for mediating a saccade, they cease discharging and allow burst cells to fire. Dysfunction of these pause neurons lead to development of opsoclonus.

To maintain eyes on target in an eccentric position at the end of saccade, agonist muscles aquire new position command to stay there. This is done by nucleus perihypoglossus and medial vestibular nucleus which is also called as Neural integrator. It converts phasic input into tonic output.

Cerebellum and PPRF control gain of this neural integrator by positive feedback. PPRF then projects to ipsilateral abducent nerve nucleus. MLF pathway finally completes the saccade by activating medial rectus on one side and lateral rectus on other side.

Superior collicullus (SC) has some role in reflexive and orienting saccades. Basal ganglia are involved in complex memory guided saccades.

Neurons in dorsolateral prefrontal cortex inhibit unwanted saccades.

Size of saccades is determined by which neurons are stimulated in superior colliculus.

Fig 21.
The Saccade test can be carried out clinically or documented by VNG. Saccade test is a part of the VNG test systems.

Testing: The saccadic system is tested clinically by SACCADE TEST and documented by VNG saccade test. Since saccades are eye movements used to rapidly re-fixate from one object to another, the clinician can test the functional status of the saccadic system by holding two widely spaced targets in front of the patient (such as the examiner's index fingers of the two hands) and asking the patient to look back and forth between the two visual targets i.e., the examiner's index fingers.

The clinician looks at the subject's eyes to see if the eyes are moving fast enough and find out whether the eyes are fixating perfectly or not, Perfection of saccade is determined by the Velocity of the saccadic eye movement, Conjugacy of eye movement, Latency of the movement and by the accuracy/ precision with which the eyes fixate the image on the fovea.

The VNG test allows very accurate documentation of all these parameters of the saccadic system. This is not possible by the clinical tests. Test for saccades are done both in the horizontal and vertical axis as in our day to day life we need to fixate vision not only horizontally but also vertically. In defects of the ipsilateral PPRF (para-median pontine reticular formation) there is slowing of horizontal saccades and in defects of the riMLF (rostral interstitial medical longitudinal fasciculus) in the midbrain, like in Progressive Supra-nuclear Palsy, there is slowing of vertical saccades.

Saccadic System Disorders	
EXAMINATION FINDING	**INFERENCE**
Slowing of saccades/ hypometria	• Intoxication • Neurodegenerative disorders
Slowing of horizontal saccades	• Suggests brain lesions usually in ipsi PPRF (Paramedian pontine reticular formation)
Slowing of vertical saccades	• Suggests brain lesions usually in riMLF (rostal interstitial medial longitudinal fasciculus) like Progressive supranuclear palsy
Slowing of adducting saccades	• Suggests inter nuclear ophthalmoplagia
Hypermetric saccades	• Suggests cerebellum (vermis) lesions or lesions in the cerebellar pathway, e.g. Wallnberg's syndrome due to damage to the inferior cerebellar peduncle

3) Gaze holding system

The function of the gaze holding system is to maintain the stable position of gaze after the saccadic system has placed the image of visual target stationed at periphery of the visual field on the fovea. In the example above, if the guest does not enter the room and keeps standing at the door then the image of the guest will be kept fixed in the fovea by the gaze holding mechanism. For stabilizing vision at the ends of the visual field in the vertical axis also the gaze holding system is necessary. Fixating images of objects at the upper and lower ends of the visual field in the fovea is the function of the vertical gaze holding system. The faculty of gaze holding both in the horizontal as well as in the vertical axis is tested clinically by clinical GAZE TEST and precisely documented by VNG gaze test.

Testing: In the clinical test for gaze the examiner sits in front of the subject and asks the patient to fix gaze at the examiner's raised index finger held at about 25-30 degrees off the center to the left/ right/ up/ down without moving the head. The examiner looks for

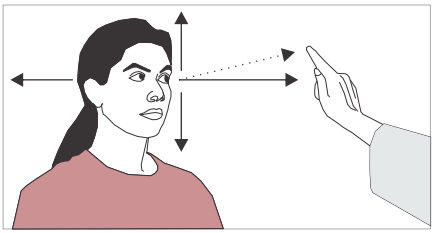


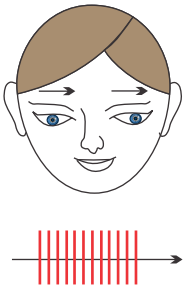
Fig 22. Four cardinal positions of gaze i.e, left, right, up and down.

any nystagmus in the subject's eyes. If there is a disorder in the gaze holding system, the examiner will see a nystagmus when the subject tries to fix gaze at the ends of the visual field but if the gaze holding function is normal there will be no nystagmic eye movement on gaze holding at a point 25-30 degrees away from the center.

Normal persons can hold the gaze very perfectly, but in disorders of the oculomotor system (central vestibular disorders) gaze holding function is jeopardized. The interstitial nucleus of Cajal (INC)controls gaze holding in vertical axis and the nucleus parapositushypoglossi (NPH) controls gaze holding in horizontal axis. Hence if in the clinical 'gaze test' or if in the VNG test of gaze there is an abnormality found in the vertical gaze then the region of the INC should be looked for and if there is an abnormality in the horizontal gaze test then a lesion in the NPN should be suspected and the radiologist should be specifically asked to look for abnormalities in these regions.

4) Optokinetic system

When we are sitting in moving car and looking outside, we see the entire visual field is moving, yet then any normal person can read the roadside hoardings, the milestones, the names of the different shops, name plates etc. The optokinetic system allows us to keep images in the fovea when the entire visual field is moving.



Optokinetic tracking

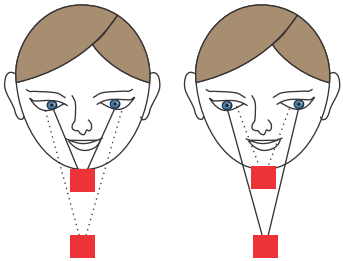
Testing: Clinically this can be tested by rotating a drum having alternate black and white stripes in front of the patient ***(Fig 23)*** or better still by the optokinetic test on VNG. VNG accurately records the speed of slow phase of the induced nystagmus. A normal person will have nystagmus when looking at the rotating stripes the speed of which will more or less be the same as that of the speed of the rotation of the stripes. Persons with defects in the optokinetic system will have a poor nystagmus the speed of slow phase of which will be much lesser than the speed of the optokinetic stimulation or in severe abnormalities there may not be any nystagmus generated at all.

The optokinetic response is a combination of a saccade and smooth pursuit eye movements. It is seen when an individual follows a moving object with their eyes, which then moves out of the field of vision at which point their eye moves back to the position it was in when it first saw the object. The optokinetic response allows the eye to follow objects in motion when the head remains stationary (e.g., observing individual telephone poles on the side of the road as one travels by them in a car, or observing stationary objects while walking past them).

Fig 23. Optokinetic test.

5) Convergence divergence system

In another complex visual scenario, supposing the subject is looking at a person who is walking away straight from the subject, then there will be a divergence mechanism of the optokinetic system will keep the image of the visual target (i.e., the person walking away) constantly fixed in the fovea whereby the subject's eyes will diverge to move apart. In the opposite scenario where the person (visual target) is coming towards the subject then there will be a convergence system where the subject's eyes will converge to come closer.

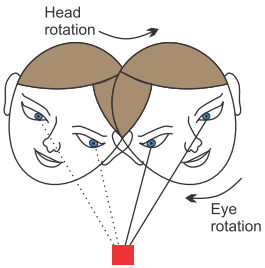


Convergence diversion

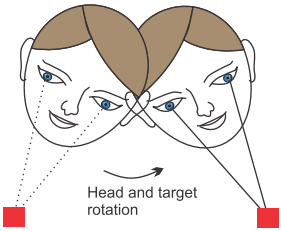
Testing: Clinically this is tested by asking the subject to look at the examiner's raised index finger which is brought towards the nasion of the subject (testing the convergence system) and then taking the index finger away from the subject's nasion (testing the divergence system). In the former the subject's eyes will converge towards the nasion and in the later the subjects eyes will diverge/ move away from the nasion.

6) VOR and suppression of VOR by visual fixation

Whenever a normal subject moves the head in any direction, the vestibular labyrinths are stimulated and the vestibulo-ocular reflex (VOR) is automatically elicited. When the VOR is elicited there is generation of nystagmus. The eyes will move slowly in the direction of head movement (slow phase of nystagmus) and fast in the opposite direction (fast phase of nystagmus). This is normal. If the head is moved from right to left there will be a right beating nystagmus as the eyes will move slowly to the left with the head at the speed of head movement but will be brought back to the center by a fast rightward movement generated by the CNS. But this nystagmus is not visible to the examiner when the subject's eyes are open as this nystagmus is suppressed by a central (i.e., CNS) mechanism called suppression of the vestibulo-ocular reflex (VORS).



Vestibulo-ocular reflex (VOR)



VOR cancellation

This suppression of the VOR and consequently the cessation of the generation of nystagmus when the head is moved with the eyes open helps in fixating the gaze and is one of the oculomotor mechanisms of gaze stabilization during head movement with eyes open. Had this CNS induced mechanism of suppression of the VOR not been functional, then nystagmus beating opposite to the direction of head movement would be generated. Consequently, visual objects would appear to be moving in a direction opposite to that of the head movement whenever we would have moved our heads in any direction and we would have felt vertiginous. This does not happen as we have this oculomotor system of suppression of the VOR by virtue of which the nystagmus is suppressed by visual fixation and this is the reason why the examiner watching the subject's eyes (which are open i.e., fixed visually) does not see any nystagmus when the subject moves the head.

But if the subject is without visual fixation (i.e., with closed eyes or if the eyes are open but are vision denied by a covered VNG goggles) then the examiner will be able to perceive the nystagmus in the subject's eyes as

the subject moves the head. The reader can try it on himself by closing the eyes and keeping his index and middle finger on the eyes and then moving the head from side to side. A jerky eye movement will be felt in the fingers which is the generated nystagmus. But when the eyes are open i.e., vision is fixed on some visual target, and then no nystagmus is generated because of the VORS.

Testing: In central oculomotor disorders, the VORS is jeopardized and visual fixation does not suppress the nystagmus generated by head movement and hence head movement with eyes open causes vertigo which is abnormal.

Fig 24. Vestibulo-ocular Reflex

Fig 25. Suppression of VOR by visual fixation

This mechanism can be tested by VNG as well as by the oculomotor tests that are now possible in some of the current versions of VHIT like the ver.4 model of the Otometrics VHIT.

Clinically the functional status of the VORS is tested by asking the subject to hold the two thumbs together with the arms extended and eyes focused on the two thumbs and then moving the head as well as the thumbs together harmoniously ***(Fig 25)***. No nystagmus will be visible in the subject's eyes if the VORS is functional, but if the VORS mechanism is non-functional then there will be a nystagmus visible to the examiner/ clinician in the subject's eyes. Test of VOR and VORS is very important in the assessment of all balance disorder patients.

EYE MOVEMENTS				
EYE MOVEMENTS	**Saccades**	**Pursuit**	**Optokinetic reflex**	**Vergence (convergence/ divergence)**
FUNCTION	To rapidly place a new object of interest on fovea	To maintain image of a smoothly moving target on fovea	To maintain eye position with respect to head and body position	To align visual axes to maintain bifoveal vision
STIMULUS	Entry of an object of interest in the periphery of the visual field	To track image of an object moving across visual field	To keep focus when the entire visual field moves	Retinal disparity/ retinal blur
LATENCY	200 msec	125 msec	10 msec	160 mesc
VELOCITY	Averages 400 degrees/sec	Averages 30 degrees/sec	300 degrees/sec	20 degrees/sec

Summary

These are all the different oculomotor mechanisms which work with the vestibulo ocular system to keep images of visual targets in the fovea and each of these systems need to be tested individually and very precisely because if any of them are not functioning properly, the patient will have vertigo or imbalance. Videonystagmography (VNG) is a complete diagnostic system for recording, analyzing, and reporting eye movements using video imaging technology, in which hi-tech video goggles with infrared cameras are used. However the clinical tests described above are also quite informative and are to be carried out in all patients presenting with balance disorders and not having a VNG machine in the clinic is not an alibi for missing out the abnormalities in the oculomotor system.

Oscillopsia

In order to achieve clear vision, objects projecting onto retina have to be stationary and perfectly stable, otherwise vision is blurred, the visual images appear unstable and there is drastic loss of visual acuity. When images of objects in the retina are not stationary and appear to be oscillating and/ or jumping, the condition is called oscillopsia which is a very incapacitating condition for the patient. When for any reason the oculomotor system is affected, the gaze holding in the retina is imperfect and this gives rise to ocsillopsia which in very mild form appears as a mere blurring of the visual field when in motion like while walking but in severe cases the entire visual field appears to be jumping as the patient moves the head while walking. The gain of the vestibulo-ocular reflex (VOR) is generated in the oculomotor system from the information obtained from the vestibular labyrinths. If the gain of the VOR is very low either due to a defect in the vestibular labyrinths or due to a defect in the oculomotor system, there will be oscillopsia. Stability of images in the retina is maintained by the ocular fixation system, the vestibulo-visual fixation system and the neural integrator. The ocular fixation system is a mechanism that operates through the cerebellar and oculomotor feedback loops to dampen and neutralize any oculomotor noise (micro-stimulations of the oculomotor system) that is caused by micro-tremors/ micro-saccades or slow micro drifts that we always perceive; but these should not cause any stimulation of the oculomotor system. If this dampening effect is dysfunctional then ocular stability is not maintained and a mild ocsillopsia is expected. Pursuit and optokinetic eye movements

are elicited by visual motion whereas vestibular eye movements (VOR) are generated by head motion. These two systems work synergistically to maintain visual stability during motion. An example of this is when a person rotates with eyes open while gazing at the surrounding environment e.g., passenger looking out of bus which is turning a corner of the road. This is the vestibulo-ocular stabilizing system and if it is defective the stability of images in the retina is compromised. In a different scenario when a person looks at visual objects that rotates with him/ her, e.g. a passenger reading a book on a bus, however the visual and vestibular systems are said to be in conflict. In this case instead of collaborating with the VOR, the visual input actually suppresses the VOR to maintain stability of the visual image in the retina. If this inhibition or suppression of the VOR fails then also there is oscillopsia. There is another complex mechanism involved in the maintenance of stability of the visual image in the retina which is called the neural integrator. Its function is to maintain constant neural innervations of the extra-ocular muscles and avoid any drift of the eyes. A defect in this neural integrator can also cause loss of stability of the image and lead to oscillopsia. Oscillopsia can occur during movement of the head if there is a bilateral vestibular failure; it can also occur at rest i.e., without head movement paroxysmally in cases of Vestibular paroxysmia and in Superior oblique myokymia and also persistently if there is any pendular/ down/ up beating nystagmus.

The Cerebellum in Maintenance of Balance

In lesions of the cerebellum also gaze stabilization is defective since the fine tuning of the contraction of the extra-ocular muscles is effected by the cerebellum as already elaborated. Lesions in the cerebellum cause abnormalities not only in the vestibulo-ocular reflex (VOR) but also in the vestibulo-spinal reflex (VSR). The cerebellum basically has an inhibitory function and there is usually an excessive eye movement in cerebellar disorders. Most balance disorders are due to problems in Floculus of the cerebellum but in defects of the other parts of the cerebellum there is vertigo/ imbalance also.

The cerebellar function therefore needs to be evaluated in all balance disorder patients. The routine cerebellar tests like finger nose test, heel knee test, test for dysdiadokinesia etc. are hence mandatory in all balance disorder patients. VNG abnormalities in the saccade test, test for smooth pursuit and other oculomotor tests should arouse suspicion of a defect in the cerebellum also as the final movement of the eye is engineered and fine-tuned by the cerebellum. If there is a cerebellar defect then all eye movements will be faulty even if the oculomotor system is normal. In cerebellar disorders the abnormality found is on the same side as that of the cerebellar lesion i.e., a left cerebellar lesion will cause abnormalities on the left movements.

Manifestations of cerebellar lesions

Vermis lesions cause...	*Flocullus lesions cause...*	*Nodulus lesions cause...*
Dysmetric saccade like hypermetria	Defect in smooth pursuit	Periodic alternating nystagmus
Downbeat nystagmus	Impaired VOR suppression and/ or positional nystagmus	Central positioning nystagmus
Gaze evoked nystagmus	Rebound nystagmus	

CEREBELLAR CONTROL OF OCULAR MOVEMENTS

The cerebellum coordinates the ocular motor system to drive the eyes smoothly and accurately and is richly supplied by afferent fibers conveying ocular information from vestibular system, afferent visual system, PPRF.

1) Dorsal vermis and fastigial nuclei determine accuracy of saccades by modulating saccadic amplitude also, they adjust innervations to each eye selectively to ensure precise conjugate movements. Lesions of these structures result in saccadic dysmetria (often overshoot dysmetria that is greater centripetally), ***Macrosaccadic oscillations*** and disorders of vergence.

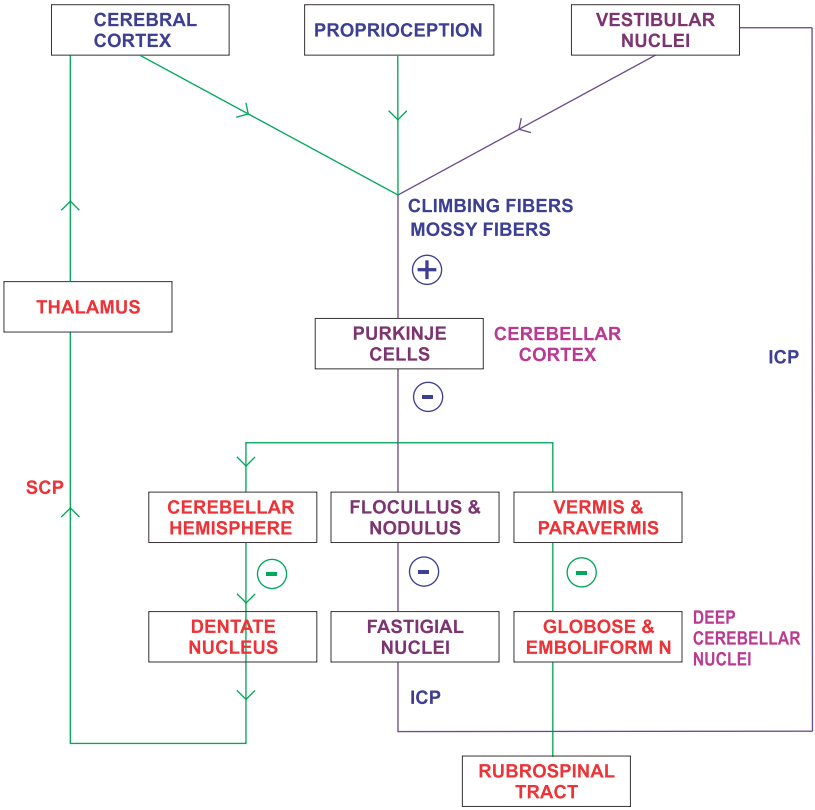
2) Flocculus - it is a part of vestibullo-cerebellum which is responsible for matching saccadic pulse and step appropriately and for stabilizing images on fovea. Lesions of the flocculus result in gaze holding deficits, such as ***gaze evoked, rebound and downbeat nystagmus***. Floccular lesions impair smooth pursuit, cancellation of VOR by pursuit system during combined head and eye tracking.

3) *Nodulus -* lesions of cerebellar nodulus cause loss of GABA mediated inhibition from the purkinje cells to vestibular nuclei leading to instability in velocity storage mechanism. Post rotational response is excessively prolonged leading to ***periodic alternating nystagmus.*** Some authorities believe that lesions in the nodulus may also cause central positioning nystagmus.

4) Deep cerebellar fastigial nuclei dysfunction leads to ***pendular nystagmus.***

It is estimated that approximately 5% or more cases of acute vestibular syndrome are due to stroke (cerebro-vascular accident - CVA). Acute vestibular syndrome (AVS) is defined as a sudden onset of dizziness or vertigo that develops over seconds/ minutes/ hours and is accompanied by vegetative symptoms like nausea and vomiting and gait instability, nystagmus, intolerance of head motion and persists for more than a day. It is usually due to vestibular neuritis, labyrinthitis, or other causes of acute peripheral vestibulopathy, but as mentioned, about 5% (some centers claim 2%) due to an ischemic stroke (CVA) of the cerebellum or brainstem. Identification of stroke is crucial as initiation of prompt treatment is of paramount importance. A stroke anywhere in the brain from inner ear to cerebral hemisphere may affect vestibular pathways but the vestibular system gets affected mostly in strokes of the posterior circulation.

Cerebellum: a key structure in maintenance of posture



Cerebellum has to and fro communications with three key systems of the body. They are cerebral cortex, vestibular system and proprioceptors. All of them provide valuable inputs related to body postures, eye and head positions of an individual. Cerebellum is connected by means of three peduncles (superior, middle and inferior) with the Midbrain, Pons and Medulla respectively. Superior cerebellar peduncle (SCP) is the main efferent pathway while inferior cerebellar peduncle (ICP) is the main afferent pathway which is in comprehensive connection with vestibulocerebellum. All afferent fibers (climbing, mossy) reach purkinje cells in the cerebellar cortex. This connection is excitatory. Various areas of cerebellar cortex then project to deep cerebellar nuclei. This connection is inhibitory in nature. Flocculonodular system in particular project to fastigial nucleus which in turn has feedback pathway with vestibular nuclei via inferior cerebellar peduncle (ICP). Cerebellum and cerebrum form a continuous feedback loop via dentate nucleus and thalamus. These dedicated circuits help in constant modulation of motor activity.

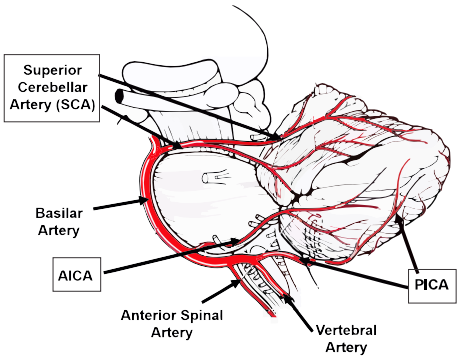
The cerebellum is supplied by three arteries: anterior inferior cerebellar artery (AICA), posterior inferior cerebellar artery (PICA) and superior cerebellar artery (SCA). They all belong to the posterior circulation. In contrast to conventional belief, the common cerebellar signs, such as dysarthria, dysmetria are frequently absent in circumscribed cerebellar infarctions. Hence absence of typical cerebellar signs in a case of acute vertigo does not rule out a cerebellar stroke.

BLOOD SUPPLY OF CEREBELLUM

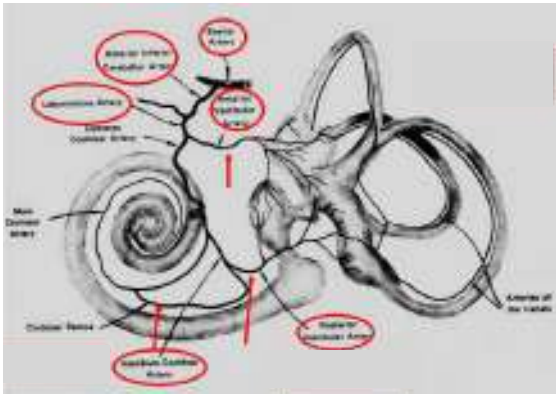
1) Superior cerebellar artery (SCA) from basilar artery

2) Anterior inferior cerebellar artery (AICA) from basilar artery

3) Posterior inferior cerebellar artery (PICA) from vertebral artery



BLOOD SUPPLY OF VESTIBULAR LABYRINTH



Blood supply of the vestibular labyrinth showing the supply of the anterior inferior cerebellar artery (AICA) separately. If the AICA is blocked then acute auditory symptoms (deafness) along with vestibular symptoms (vertigo) will be present as both the labyrinthine artery and the anterior vestibular artery will be deprived of blood supply. The anterior vestibular artery is an end-artery; hence ischemia/ infarction of this artery is possible causing damage to the anterior and lateral semi-circular canals only and causing acute isolated vertigo with no auditory symptoms or other neurological symptoms. Cochlear branch of the common cochlear -- posterior vestibular artery supplies the basal turn of the cochlea (where high frequencies are processed). Hence hearing loss in association with ischemic processes on the vestibular nerve is usually involves the high frequencies.

BLOOD SUPPLY OF CEREBELLUM

Features	PICA	AICA	SCA
Origin	Verterbral artery	Proximal to midbasilar artery	Distal basilar artery
Branches	Medial, lateral	**Internal auditory artery**	Medial, lateral
Key brainstem structures supplied	Poterolateral medulla Cranial nerve nuclei (V,VIII,IX,X) Sympathetic tract Inferior cerebellar peduncle	Posterolateral pons Cranial nerve nuclei (V,VI,VII) Sympathetic tract Middle cerebellar peduncle	Posterolateral midbrain Cranial nerve nuclei IV,V Medial leminiscus Superior cerebellar peduncle
Cerebellar structures	Posteroinferior cerebellum Uvula, **nodulus**	Anteroinferior cerebellum **Flocculus** Inner ear, labyrinth, cochlea	Superior cerebellum **Dentate nucleus**
Core feature	**Pseudo vestibular neuritis** Lateral medullary syndrome	**Pseudo Labyrinthitis** Lateral pontine syndrome	Acute gait and trunk instability Lateral midbrain stroke

In the initial stages of a stroke (i.e., central type of acute vestibular syndrome) of the brainstem or cerebellum there are usually no neurological signs/ symptoms, and central acute vestibular syndrome (cAVS) mimics the peripheral types of acute vestibular syndrome (pAVS). Imaging studies are not very informative in the initial stages and a normal MRI or absence of neurological signs does not rule out cAVS. The best way to identify a cAVS in the initial stages is the clinical head impulse test (HIT). Where available, a video head impulse test is obviously more helpful. In cAVS, the head impulse test is negative but in pAVS, the head impulse test is positive (i.e., abnormal saccades are present in the HIT). The sensitivity and specificity of HIT is nearly 100% if it is a stroke of the posterior inferior cerebellar artery (PICA) where there is cerebellar stroke. But in a stroke of the anterior inferior cerebellar artery (AICA) the lesion is in the root entry zone of the 8th cranial nerve and the HIT is positive. Hence PICA strokes involving the cerebellum or lateral medulla are easily identifiable by the negative HIT but AICA strokes are liable to be missed just by the HIT. Another bedside clinical test for identification of cAVS is direction changing nystagmus in lateral gaze. The third predictor for cAVS is test for skew deviation which is a reliable clinical test that can be carried out at the bedside. In cAVS the test for skew is mostly, if not always positive. The alternate cover test and the clinical findings of the head tilted to one side and one eye at slightly higher level than the other eye is a sign of positive skew test. It occurs due to disparity of the otolithic inputs from the vestibular labyrinths to the oculomotor system. The three tests together i.e., the head impulse test, test for nystagmus and test for skew is called the HINTS test.

Bedside HINTS test is a very useful tool for differentiating acute central vascular vertigo from more benign lesions involving inner ear.

HI - Head impulse normal
N - Direction changing nystagmus
TS - Test of skew deviation(present)

The HINTS test showed 100% sensitivity and 96% specificity in identifying strokes in patients with acute prolonged vertigo lasting more than 24 hours. However, HINTS is not be sufficiently dependable to detect AICA infarctions as HINTS is positive in this disorder as explained. In the initial stages of acute vertigo, it is much more sensitive than diffusion weighted MRI for differentiating cAVS from pAVS.

Postural Stabilization

The second function of the vestibular system is postural stabilization. Postural Stability is the process by which we stay erect without falling and involves the faculty by virtue of which we maintain our posture without falling down. It is tested by Computerized Dynamic Posturography (CDP), Stabilometry, Cranio-corpography (CCG). We require this faculty of postural stabilization for routine daily activity in our day to day life for standing, walking, suddenly turning, running and in all forms of locomotion. Balance is the faculty of maintaining erect physical posture, movement is the faculty by which we move body parts and locomotion is the faculty by which the body moves from one place to another. Walking is one form of locomotion. Balance is the very basis of postural stability and locomotion. Maintenance of erect posture in different types of surfaces like an even hard surface or an uneven gravel is again a function of the vestibular system i.e., the postural stability. If this faculty is defective locomotion is jeopardized.

The pyramidal and extrapyramidal pathways, the cerebellum, the ascending and descending tracts in the spinal cord, the peripheral nerves that connect the spinal cord to the voluntary muscles of the trunk and limbs and finally the muscles play an important role in the maintenance of postural stability. A defect in any one of them can jeopardize this vital function of the balance system. Some details of these have been elaborated in the previous sections.

The goal of postural stabilization is the maintenance of erect posture in static & dynamic conditions both in routine daily activities as well as in complicated activities like cycling/ playing badminton/ other sports activities/ dancing etc. It executes spontaneous balance correction when there is a destabilizing force acting on the subject and also helps in balance stabilizing response in volitional destabilizing actions like sporting activities. The process involves the cerebellum and the descending pathways like the pyramidal and extrapyramidal tracts from the motor cortex to the skeletal muscles of the limbs/ trunk and the neck.

Mechanism of maintenance postural stability

The narrow base of support and multi-segmental body architecture results in a potential instability of the erect posture. Postural stability involves the synchronization of strategies to stabilize the center of body's mass during disturbances of stability induced by external destabilizing forces as well as by those initiated by the subject himself. The exact response strategy chosen by the body's balance mechanism to counter the destabilization depends not only on the characteristics of the postural displacement induced by the external destabilizing force (or self-induced like while dancing) but also on the particular person's objectives, expectations of the outcome and also on prior experience which is retrieved from the vestibular memory at that particular time. Anticipatory adjustments of posture and stance before initiation of movement of the trunk or the limbs helps to sustain postural stability by counteracting and responding to the destabilization associated with moving the trunk or the limbs.

All this requires a huge amount of cognitive processing, as determining the best anticipatory postural adjustment and the selection of the best strategy that is most suited for a particular form of destabilization depends on the cognitive skills of the person. The extent of cognitive processing required for postural control depends both on the complexity and nature of the destabilizing force and on the proficiency of the subject's posture control system. Cognitive deficiencies that occurs in old age hence leads to postural imbalance and falls. Multiple mechanisms are involved in postural control/ stabilization which are more complex but less studied than gaze stabilization. Too many biological mechanisms and processes are involved in the control of posture and even a sub-clinical constraint not necessarily a full-fledged pathology can jeopardize the mechanism of maintenance of postural stability.

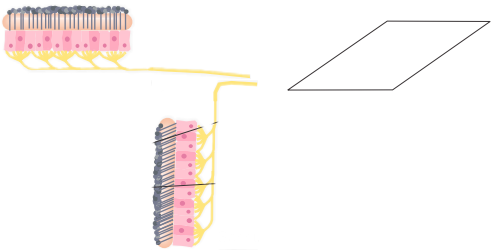
Perception of Visual Vertical and Graviception

The third function of the balance system is perception of verticality or graviception. It is the sense of verticality and the correct feeling of the line of the force of gravity acting on the body. To keep ourselves erect and to feel that we are not tilted or unsteady, the correct perception of the line of gravity is essential. This is a vestibular function, and has been elaborated in page 35-37 of this book. For proper orientation of the visual surroundings and for getting the sense of self localization in three dimensional space, the brain perceives the co-ordinates of verticality and horizontality and on the basis of this perception we get the feeling of how we are oriented or placed in relation to the surroundings. To get the correct orientation our perception of verticality i.e., what we consider as vertical has to perfectly tally with the gravitational vertical . The sense of horizontality is at right angles to our perception of verticality. If the sense of verticality is deranged the sense of horizontality is also correspondingly deranged and what we see will appear tilted. Not only that we will also get a feeling that we are not standing straight and that our body is tilted.

This creates a marked sense of instability and gives the sensation of unsteadiness which is mentally very traumatic. Correct perception of the vertical & horizontal i.e., the perfect sense of graviception gives us the correct orientation relative to gravity and is also instrumental in determining direction/ trajectory and speed of movement of a visual target.

Otolithic Function

This perception of verticality is an otolithic function. The otolithic organs ***(Fig 26)*** in the vestibular system sense gravity. Both the utricle and saccule contribute to the sense of verticality. So, if the otoliths, or the nerve that transmits impulses from the otoliths and other parts the ear to the brain, is damaged, judgment of verticality may be altered. The inner ear may falsely suggest that the head is tilted while the eyes and somatosensory systems suggest that one is upright. Thus there is a sensory conflict.



There can be an interaction between vision and the otoliths in that an otolith imbalance may transiently cause the eyes to counter-roll, which literally tilts ones vision. In the otolith organs we have the macula just like the ampulla in the semicircular canals. It is the sensor for the organ. Stimulation of the macula elicits the maculo-ocular and the maculo-spinal reflexes. The ***maculo-ocular reflex*** brings about ***gaze stabilization*** and the ***maculo-spinal reflex*** brings about ***postural stabilization.*** Both together carry out the function of the perception of verticality. The defect in the VOR induced by the faulty maculo-ocular reflex leads to skew deviation of the eyes and to ipsilateral ocular cyclo-torsion which are clinical signs that an astute clinician can pick up provided he carefully looks for it.

the force of gravity and what is away from the force of gravity and the maintenance of the muscle tone of the anti-gravity muscles by the contraction of which we stay erect and oriented in the line of the gravitational vertical is carried out by the otolith organs. The correct muscle tone of the graviceptive muscles needs to be maintained to counteract the force of gravity pulling the subject down and thereby preventing a fall and this tone of the anti-gravity muscles is maintained by the inputs of the otolith organs. This combined with the correct perception of verticality is required for maintenance of the correct erect posture and for the subject to feel that he is properly oriented in three dimensional space. Not only that, inputs from otolith organs and other graviceptors play an important role in regulating blood pressure during changes in posture.

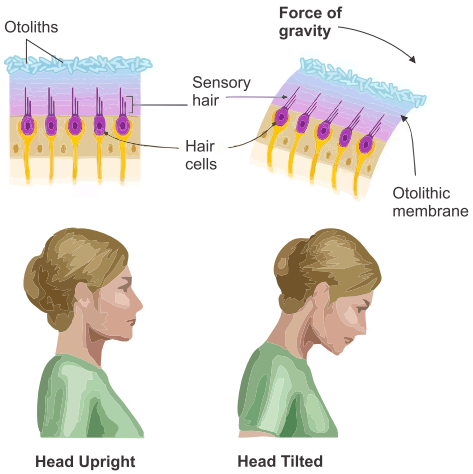


Fig 27. Otolithic function

OTOLITHIC FUNCTION

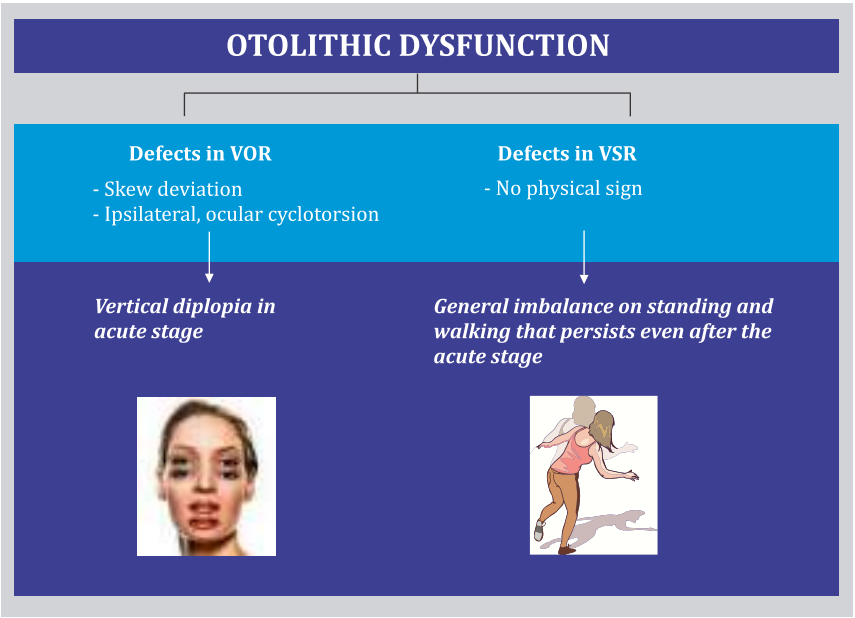
Maculo-Spinal Reflex	Maculo-Spinal Reflex
(Maintains postural balance e.g. train suddenly stops the subject does not fall)	(Stabilizes gaze during head movement laterally & vertically)

Maculo-spinal reflex & Maculo-ocular reflex both become defective in otolith dysfunction.

Otolithic Dysfunction

In otolithic dysfunction the otoliths provide erroneous information for control of posture and gaze stabilization in horizontal and vertical planes. This leads to incorrect sensation of upright posture, of a sense of self-motion and an incorrect spatial orientation of the body.

This is traumatic for the subject both physically and mentally and the subject complains of a strange feeling of disorientation rather than rotating/ spinning, a feeling of instability and psychological disturbances like panic/ anxiety. The feeling of self-motion and incorrect spatial orientation of the self are by themselves extremely traumatic mentally and induces a sense of insecurity lack of self confidence, anxiety, apprehension of losing balance and panic attacks. In general, otolithic disorders induce instability unlike the semicircular canal disorders which induce more of vertigo.



Subjective Visual Vertical Test (SVV)

The Subjective Visual Vertical Test (SVV) is the test to ascertain the sense of verticality of a subject. The purpose of this test is to detect abnormal subjective tilt. In the SVV test, a tilted straight line is projected from the projector on the screen in a dark room and the patient is given a joy stick and asked to make the line vertical. In normal persons, the ability to perceive verticality is normal and the subject can make the projected line absolutely vertical. The computer measures the tilt in the line after the patient has oriented it according to what he perceives as vertical and by this we can measure that how much the patient's sense/ perception of verticality has deviated to one side. This ability is dependent on input from otolith systems but also on cortical functions of the central nervous system. Otolithic function is also tested by the Vestibular Evoked Myogenic potential tests (the ocular and the cervical VEMP tests) but the subject's perception of verticality is measured only by the SVV test.

Fig 28. The NeuroEquilibrium (www.neuroequilibrium.in) SVV patient test setup with specially designed goggles for tubular vision.

A ceiling mounted projector projects an illuminated line on the wall/screen in a darkened room. The subject is given a joystick (the same used for computer games) or a remote control with which the subject can tilt the line both ways. An eye-wear (googles) restricts the subject's field of vision such that the vision is narrowed to a circular area in the center of the screen and any external reference surrounding the screen is excluded. The computer software tilts the line at random and the subject is asked to align the line vertically each time. The software calculates the deviation The test is repeated a number of times (at least 10 times) and the average tilt calculated. Any tilt beyond 2.5 degrees is considered abnormal. The test can be made more difficult by optokinetically stimulating the background and then asking the subject to align the line vertically against the backdrop of the rotating spots.

Central and Peripheral Disorders

From the clinical perspective, vertigo and imbalance can be caused by disorders in the brain or by disorders in the vestibular labyrinths, the eyes, some sensors called proprioceptors in different parts of the body and also by disorders in the neural connections between all these different organs. Those caused by disorders in the vestibular labyrinths are conventionally called peripheral disorders and those caused by disorders in the brain (and ? the other organs) are called central disorders. A patient having a disorder in the eyes/ in the peripheral nerves of the lower limbs should strictly be labeled as a peripheral disorder but conventionally it is not considered so.

The demarcation between central and peripheral is rather vague and though the age old teaching has been to try to identify whether a patient presenting with balance disorder is a central or a peripheral lesion, this does not have much clinical relevance today. For proper management just a differentiation between central and peripheral is of no clinical significance. Most peripheral disorders will induce some functional central changes and vice versa. Any acute lesion in the vestibular labyrinth will induce some changes in the brainstem for the development of vestibular compensation and the final outcome will be a combination of the peripheral lesion plus the corresponding functional change in the brain.

Gone are the days when peripheral disorders used to be treated by eternal vestibular sedatives and central disorders managed by imaging studies followed by a neurological referral and then quite often some vague/ irrational medication not uncommonly the same old vestibular sedatives or some drugs like citicholine or methylcobalamine or ginkgobiloba or rarely drugs like sodium valproate or piracetam often empirically prescribed. Today's understanding of vestibular physiology and the tests and investigations to identify and localize a lesion structurally and functionally and the treatment thereof is so very precise and organ-specific that such broad demarcations between central and peripheral are actually irrelevant.

Today's neurotologist hunts whether there is a lesion in the utricle in the vestibular labyrinth or in the anterior semi-circular canal and if so, on which side and at what frequency of vestibular stimulation is the specific organ malfunctioning or is there a lesion in the basal ganglia or in the flocullus of the cerebellum, whether the mechanism of suppression of the vestibulo-ocular reflex or that of smooth tracking is jeopardized. Tests both clinical and instrumental available today if coupled with a detailed history-taking offers the finesse and precision of a very perfect pin-pointed localization of the site of lesion and also the diagnosis of the causative pathology. There are very specific therapies for each of the disorders. If the disorder is caused by positional vertigo of the left lateral semicircular canal there is a specific therapy for it in the form of a liberatory maneuver; if there is a lesion in the right utricle there is a specific therapy in the form of a specific physiotherapy for stimulating the utricle; if there is a stroke in the cerebellum there is a protocol for stroke management etc.

Lastly, vertigo is something where some people will get a 2 second vertigo on lying down in bed just for a few days but this is so much of a psychological trauma to them that as long as they live they will in fear to lying down in bed and may spent the rest of their lives sitting on couch at night. And some people will go to an amusement park, pay money to enjoy the vertigo. The sensation of vertigo is pleasure to some and dreadful for some. Why does this happen? We do not yet fully understand. There is hence a huge psychic component in vertigo which complicates the picture and is one of the grey areas not yet fully understood.

Nevertheless in the last two decades our understanding of the mechanism of balance has undergone a sea change and we are now in a much better position to understand the underlying changes in the functioning of the balance system when diseased and hence can effectively manage most forms of balance disorders very scientifically and logically.

In Vertigo of Mixed Origin

℞ VERTIGEN

Cinnarizine 20 mg + Dimenhydrinate 40 mg

The FIRST-LINE Antivertigo Therapy

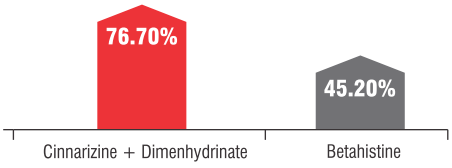
Established Efficacy

Effective control of both vertiginous and vegetative symptoms[1]

- **61%** — Improved Vertigo Symptoms (Dysstasia, Walking unsteadiness, Staggering and rotatory sensation)
- **84%** — Nausea
- **85%** — Vomiting
- **51%** — Tinnitus

Established Safety

Better tolerability than Betahistine[2]



Dosage : **1 Tablet T.I.D for 4 weeks**[3]

1.Wien Klin Wochenschr DOI 10.1007/s00508-015-0905-5 2.Clin Drug Invest 2012; 32 (6): 387-399 3.Clinical therapeutics Vol. 26. No. 6. 2004: 866-877