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Physiology of vestibular system

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Introduction:

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All the sensory systems should be interpreted in view of the survival of the species. In this regard the mammalian vestibular system generates information and feeds them to the brain. The information thus fed to the brain encompasses the following parameters:

1. Gaze stabilization to ensure the field of vision stays focused on the object of interest

2. Body position & locomotion to enable balanced locomotion without compromising body posture

3. Orientation of the body with respect to gravity

4. For readjusting autonomic functions after body reorientation

Input systems proving this vital information to the brain include:

1. Visual

2. Vestibular

3. Proprioceptive system

4. Hearing cues (of lesser importance)

Brain processes these various inputs received leading onto various outcomes which include various reflexes and responses.

1. Vestibulo-ocular reflex VOR to ensure gaze stabilization

2. Vestibulospinal (VSR) and vestibulocollic reflexes (VCR) ensures maintenance of upright position of body and trunk and head stabilization in space

3. Orientation and in higher species, navigation and perception of self-position with respect to surroundings and gravity is mediated by vestibular cortex.

4. Autonomic function adjustments after alterations of body orientation

In addition to the above stated features, vestibular system has been shown to influence the circadian rhythm and also on cognitive functions. Circadian influence is most likely due to direct projection of the vestibular nuclei to the suprachiasmatic nucleus.

Note:

Although visual, vestibular and proprioceptive inputs are constantly processed by the brain, they are weighted by other factors, such as:

Learning

Memory

Drugs

Ageing

Environmental conditions

This is amply illustrated when walking in darkness, where balance cannot rely heavily on vision and other inputs like somatosensory and vestibular senses play a huge role.

Peripheral receptors:

There are two types of peripheral receptors:

Cristae:

These receptors are located in the ampullated ends of the three semicircular canals. These receptors respond to angular acceleration.

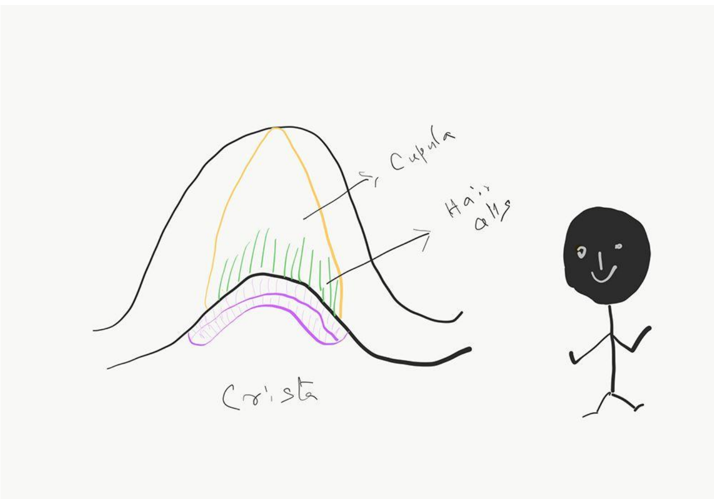


Image showing position of crista while standing

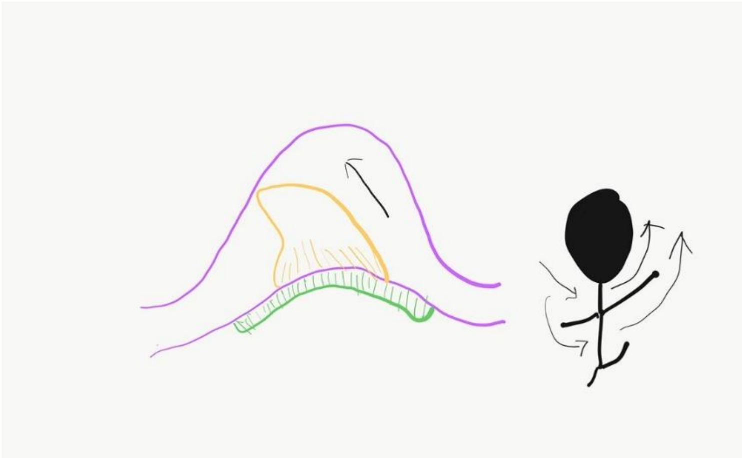


Image showing position of crista while rotating

Semicircular canals:

The movement of endolymph in the semicircular canals is the key for determination of movement of the head (nodding, or during walking and running). The semicircular canals were evolutionally adapted to sense these movements. Head acceleration triggers the sensory epithelium, the signal that is transmitted from these sensory epithelia to the brain is proportional to the head velocity. Head accelerations can rise up to several thousands of degrees per second square3, the head velocity is limited to several hundred of degrees per second. Sustained velocity is no longer detected nor perceived after 30 seconds.

Passive forms of movements like in aero planes, merry-go-rounds, cars, rollercoasters generate more intricate movements and can readily induce motion sickness since the vestibular apparatus is not adapted to these kinds of motions.

Semicircular canals allow movement of endolymph only in the direction along the cylindrical canalicular cavity. When SCC are rotated about an axis, three forces act upon the endolymph and cupula in the canal. These include:

1. The inertial force, proportional to the mass of the endolymph and cupula.

2. The elastic restoring force of the cupula that positions the cupula back to the center position after stimulation.

3. The viscous forces that act upon the fluid when sliding past the internal wall of the tube. This force is dependent on the speed of relative movement of endolymph with respect to the wall.

The cupular deflection is the signal that the brain receives, because this process triggers hair cell depolarization or hyperpolarization.

The semicircular canals are not designed for sustained rotation stimulus. Rotation at constant speeds is not sensed by the SCC after 30 seconds. Only the phases of acceleration and deceleration are detected. The cupula is restored to its centre position within a period of 12 seconds.

Crista is a crest like mound of connective tissue on which lie the sensory cells. The cilia of the sensory cells project into the cupula, which is a gelatinous mass extending from the surface of crista up to the ceiling of the ampulla forming a water tight partition, only to be displaced to one or the other side like a swing door coinciding with the movements of endolymph. The gelatinous mass of the cupula consists of polysaccharides and contains small canals into which project the cilia of the sensory cells. Nystagmus outlasts the above said phenomenon. This is because of the unique feature known as the velocity storage mechanism.

Velocity storage mechanism:

This mechanism serves to maintain the Vestibulo ocular reflex (VOR) at low frequencies (below 0.02 Hz). Vestibular storage mechanism principally uses the peripheral labyrinthine signal and by a process of integration, increases the response of the Vestibulo ocular reflex. This is done by prolonging the time constant of the decay of the vestibular nystagmus to 20 seconds. This circuitry stores neural activity related to head and eye velocity and discharges it over its own time course. This hence plays an important role in optokinetic reflex which is present during sustained rotations. This reflex takes over the fading performance of the vestibular system. The transition between VOR and optokinetic reflex is facilitated by velocity storage mechanism. The time constant of velocity storage is influenced by static inputs from the otoliths. This can be reduced considerably when the head is suddenly tilted.

Vestibulo ocular reflex:

The peripheral sensors transmit motion details to the brain through frequency encoding. This is something similar to FM radios. The brain continuously receives frequency modulated signals. A normal resting discharge rate of approximately 90 spikes / second is modulated in such a way that increase of this rate corresponds to an excitation or decrease with inhibition.

The left and right semicircular canals are oriented in the head in such a way that any movement always induces an antagonistic response in both canals.

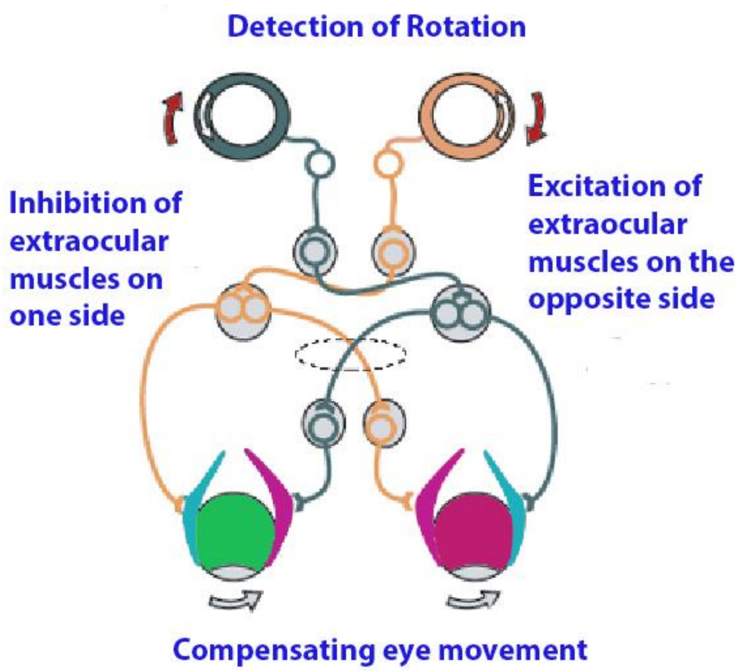


Image showing the components of Vestibulo ocular reflex

The following are the features of Vestibulo ocular reflex:

1. During head rest, hair cells in both semicircular canals have a resting discharge of 90 spikes / second.

2. Endolymph fluid lags behind within each SSC due to inertia.

3. In right sided head turning, the leading SSC (the right), the stereocilia bends towards the kinocilium.

4. During the postulated right head turn, the discharge rate increases in the leading right ear from 90 to 30 spikes / second.

5. In the following SSC i.e. the left, the stereocilia bend away from the kinocilium

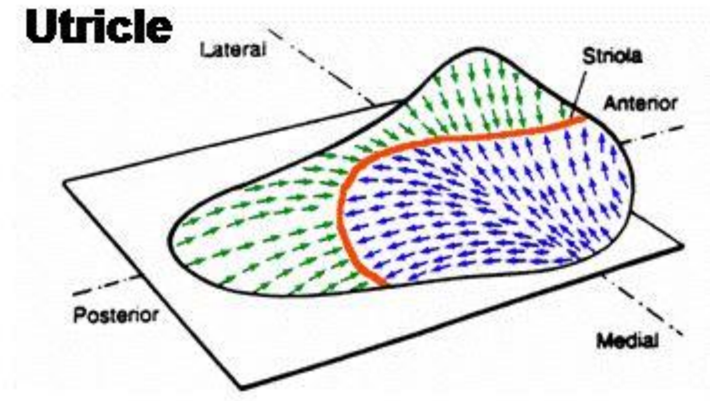
6. The discharge rate decreases in the following left ear from 90 to 20 spikes / second

7. The vestibular nuclei interprets the difference in the discharge rates between the left and right SSC's as movement towards the right, and triggers the oculomotor nuclei to drive the eyes to the left to maintain gaze stabilization.

Similar to the lateral canals, a push-pull principle is also seen in the vertical canals. The left anterior canal is excited while the right posterior canal is inhibited for the same movement. The vertical canals are direction sensitive, and ampullopetal movement results in a decreased firing rate. The ampullary deflection in the vertical canals, corresponding to excitation is in the opposite direction to the horizontal semicircular canal.

The horizontal canals are involved in pitch movements only to a small extent. The inclination of the vertical canals is more than 90 degrees to the horizontal, and so the horizontal movements are always detected also by the vertical canals. Because of the antagonistic response of the anterior and posterior SCC on each side, horizontal head movements produce primarily horizontal eye movements.

The SCC's and the otolith organs provide the inputs for the VOR. Horizontal VOR compensates for both horizontal rotation and horizontal translation. The former is due to the canal system while the latter is due to the utricular system. There are three types of rotationally induced eye movements: horizontal, vertical, and torsional. Each of the 6 pairs of eye muscles should be controlled to produce the desired response. The vertical SCC's and the saccule are responsible for controlling vertical eye movements, whereas the horizontal canals and the utricle control horizontal eye movements. Torsional eye movements are controlled by the vertical SCC's and the utricle.



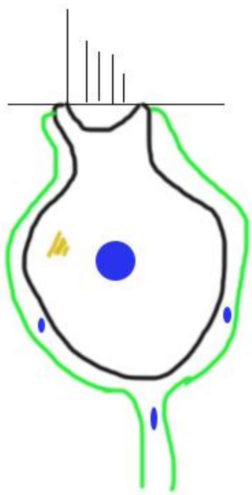
The hair cells of crista are of two types:

Type I cells:

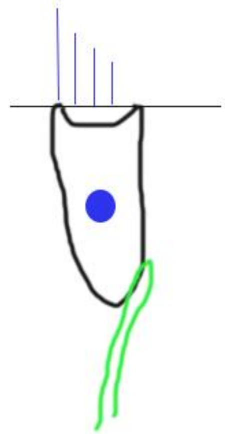
These cells are flask shaped, with a single cup like nerve terminal surrounding the base.

Type II cells:

These are cylindrical with multiple nerve terminals at the base. From the upper surface of each cell project a single hair the kinocilium and a number of other cilia the stereocilia. The kinocilium is thicker and is located on the edge of the cell. These sensory cells are surrounded by supporting cells which show microvilli on their upper ends.



Type I hair cell



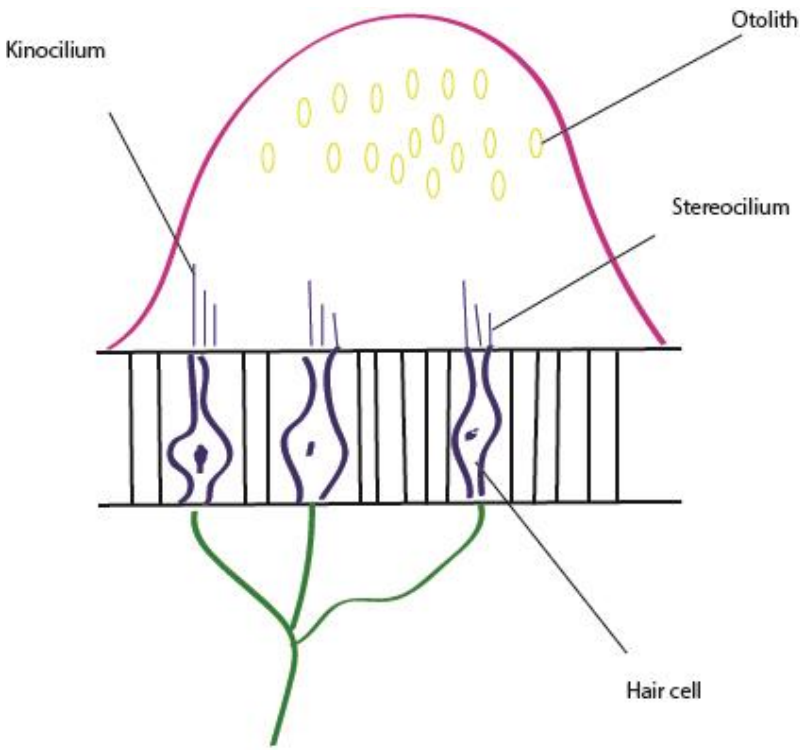
Type II hair cell

Nystagmus:

To and fro eye movements are known as nystagmus. The ocular response to a head rotation is a combination of slow phase or drift of the eye until it reaches the edge of the outer canthus, followed by a fast phase which rests the eye back to the initial position. This pattern repeats itself as long as the head rotation exists. The direction of the nystagmus is indicated by the direction of the fast reset phase as it is easy to observe by the physician. The slow phase of the nystagmus is actually defined by the actual vestibular stimulation and is quantified. In video nystagmography the upward excursion represents eye deviation to the right, corresponding to the slow drift towards the right, which is followed by the quick leftward reset saccade and is represented by the downward trace which is defined as a left nystagmus.

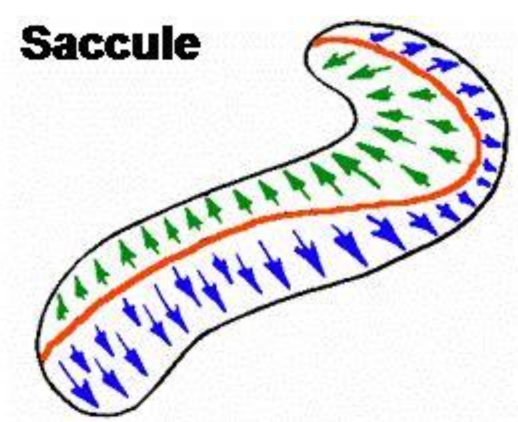
Maculae:

These receptors are located in otolith organs (utricle & saccule). Macula of the utricle lies in its floor in a horizontal plane whereas the macula of saccule lies in its medial wall in a vertical plane. These receptors sense the position of head in response to gravity and linear acceleration.



Condition of macula when head is held straight

Tonic resting activity is seen

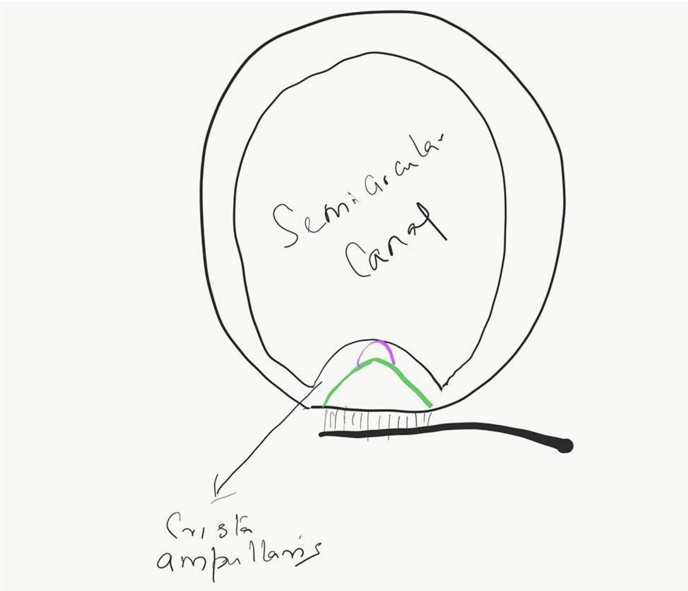


Otolith organs:

On Earth the gravitational force acts permanently and the acceleration caused by it need to be detected on a continuing basis. This role is played by otolith organs. Otolith also additionally detect all linear accelerations. These organs are designed such that they detect the accelerations and send encoded signals to the brain that processes the relayed information. The otolith organs (utricle & saccule) are oriented orthogonally to each other. The utricle is relatively horizontal, and the saccule is predominantly vertical (tangential in the head). Motion hence in the horizontal plane triggers predominantly the utricle, and vertical movements trigger mainly the saccule. Due to the curvature of these organs, they manage to detect any form of movement.

Einstein's equivalence principle states that no single physical device can distinguish gravity from linear acceleration. This really poses a difficult scenario for the central nervous system since otoliths cannot differentiate between linear acceleration and tilt since only the deflection of the base of the hair cells are encoded and sent to the brain. During natural movements (both active & passive), the otolith organs sense the sum of all accelerations acting on the head and interpret these signals to initiate postural and eye reflexes mediated by the vestibular nuclei, directing appropriate signals to the limb, trunk, and neck muscles via the vestibulospinal tracts or to the eye muscles via the Vestibulo ocular reflex (VOR). The interplay of several senses at the same time (visual, vestibular and proprioceptive) enables the CNS to cope up with the ambiguity of linear accelerations under normal conditions. However, in darkness when visual stimulus is rather useless it relies on the vestibular cues.

There is an internal model of head orientation present in the cerebellum and the vestibular nuclei, and it resolves the ambiguous gravitational cues that are measured by the graviceptors as well as with input from the semicircular canals. The signals from the otoliths and from the canals are not treated separately in the brain but are continuously combined to optimize the Vestibulo ocular reflex. This is made possible by the overlap of almost all partitions of the vestibular end organs.



Ultrastructure of macula:

It consists mainly of two parts.

Sensory neuroepithelium made up of type I and type II hair cells similar to that of crista.

Otolithic membrane made up of a gelatinous mass and on the top are seen crystals of calcium carbonate (otoliths/otoconia). The cilia of hair cells project into the gelatinous layer. The linear, gravitational and head tilt movements cause displacement of otolithic membrane and thus stimulate the hair cells that lie in different planes.

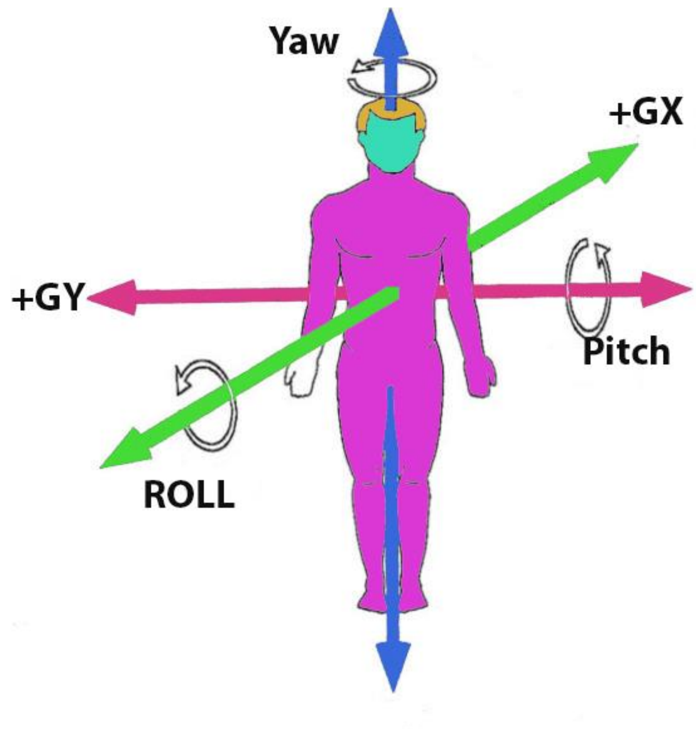
Components of motion and head orientation:

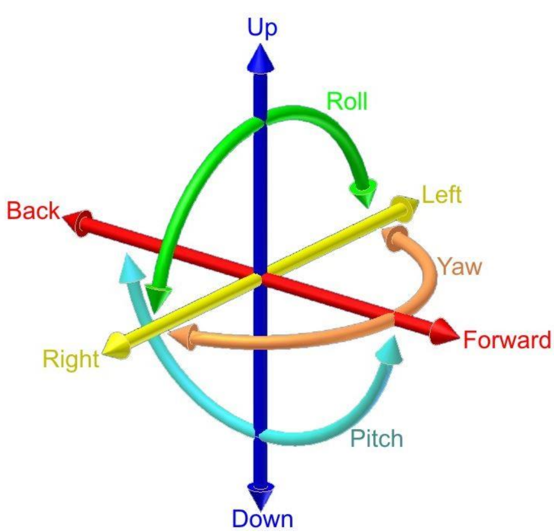
All motions in space can be broken down into three rotational degrees of freedom:

Yaw

Pitch

Roll





Images showing various degrees of freedom

And also, three transitional degrees of freedom (left-right, up-down, fore-aft). No single event in one degree of freedom can be described by the others, hence every movement is uniquely and appropriately described by a combination of all 6 degrees of freedom. The anatomical design of these motion sensors in the vestibular system reflects all these six degrees of freedom. The sensors in the semicircular canals measure predominantly rotations whereas the maculae of utricle and saccule detect mainly translations.

Some general aspects of vestibular system on both sides:

The right and left semicircular canals are parallel systems. The right anterior canal is parallel to that of the left posterior canal, and they both lie in a plane denoted as the RALP plane. Similarly, the right posterior and left anterior line in the LARP plane.

Both horizontal (lateral) semicircular canals lie parallel to each other in the lateral plane. The horizontal canal makes an angle of approximately 30 degrees up with the horizontal axis of the head. The angles of the vertical canal are approximately 45 degrees with the sagittal plane of the head.

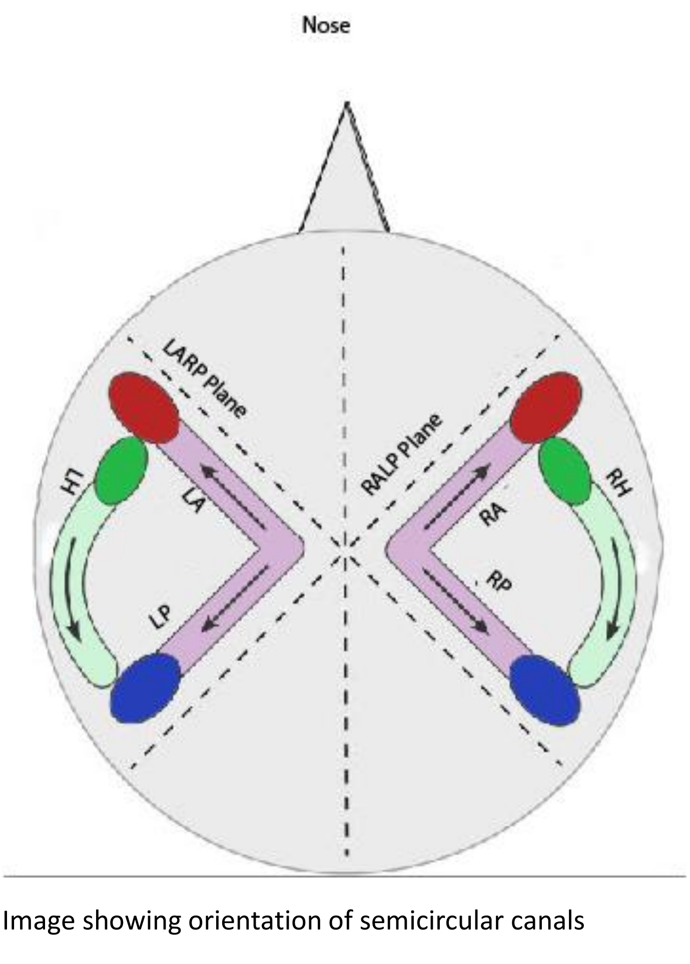


Image showing orientation of semicircular canals

Movement detection:

Basic laws of physics are responsible for detection of movement or orientation of the vestibular system. During daily life, body and head are continuously moving. These movements are always related to forces of acceleration. These movements are sensed in the vestibular system by a rigid coupling of sensory epithelium to the bony structure. Being fluid filled body, and also being attached to the skull the inertial forces drives the fluid. This motion of the fluid lags behind any motion of the head and this relative displacement is the trigger for movement detection. To limit the movement of the hair cells triggered by the forces of acceleration, the canal system is designed such that the deflection of the hair cells is proportional to the head velocity.

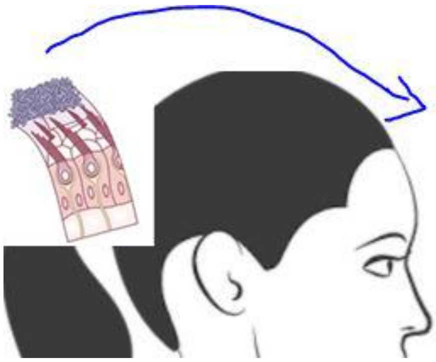
Acute unilateral deafferentation:

This occurs during acute peripheral lesions. In cases of acute deafferentation (on the right side) all three right canals and the otoliths cease spontaneous activity from 90 spikes per second to zero. Whereas spontaneous activity of the left SCC remains at 90 spikes per second. Although the head is not moving, the brain perceives an apparent imbalance (R: 0 spikes / sec versus L: 90 spikes/second). This imbalance drives the vestibular and consecutively, the ocular motor nuclei to move the eyes towards the right as would be appropriate for a head movement towards the healthy side (i.e. left) causing giddiness.

Vestibulocollic & vestibulospinal reflexes:

The pigeons while walking move their heads backwards and forwards. This movement of the head is actually a type of head nystagmus, meant for gaze stabilization and is controlled in the same manner as the VOR in higher species. In rabbits, both eye and head nystagmus are equally present.

The extraocular muscles are the effector organs for the VOR, while the extensor muscles of neck, trunk, arms and limbs are those for the vestibulocollic reflex and vestibulospinal reflex. These reflexes are usually mediated through projections of the vestibular nuclei on to the medial and lateral Vestibulo spinal tract. These pathways project to the lower limb and neck muscles to maintain an upright position and balanced locomotion. But proprioceptive and visual information is also necessary to provide the correct body position, because of the fact that gravity is only detected in the head, regardless of the position of the trunk and lower body.



Images showing the effects of forward and backward tilts on the vestibular hair cell system

Cervico ocular reflex:

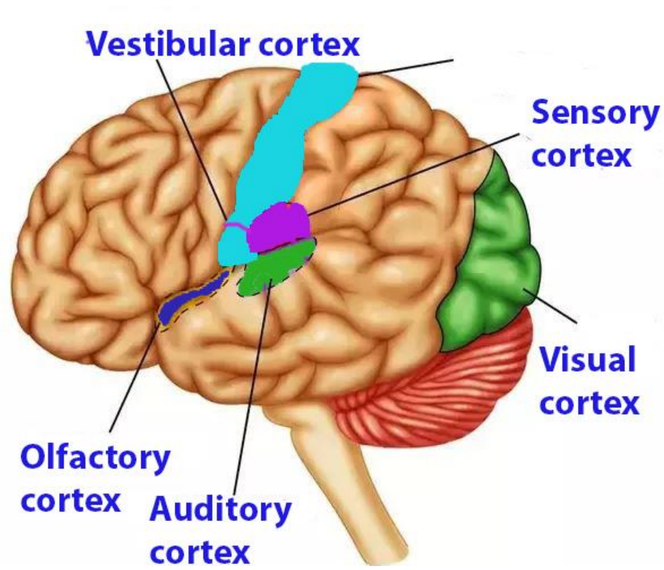
In some cases, when the head is fixed but the body is rotated, nystagmus may be observed. This reflex is based on the stimulation of neck receptors rather than vestibular receptors. In humans this reflex is very unreliable and unpredictable.

Vestibulosympathetic reflex:

Moving from supine to a standing position generates a great amount of orthostatic stress on the body due to pooling of blood (about 800ml) in the abdomen and lower limbs. Maintenance of blood supply to brain in this scenario is the responsibility of this reflex which increases the heart rate and blood pressure.

Vestibular cortex:

It is the insular cortex which is a part of the cerebral cortex folded deep within the lateral sulcus and is believed to play a main role in processing vestibular signals. Predominantly the right hemisphere plays an important role in processing vestibular signals.



Central projections of vestibular system:

Movements sensed by the vestibular organs on the right and left sides converge in the vestibular nuclei after passing through the ganglion of scarpa. The semicircular canals and otolith maculae project to different portions of the vestibular nuclei from where they trigger other brain centers so as to maintain gaze stabilization as well as body stabilization.

The vestibular nerve has two divisions:

Superior vestibular nerve: Afferents from the horizontal and anterior canals as well as from the utricular macula and anterosuperior region of saccular macula form the superior vestibular nerve.

Inferior vestibular nerve: Fibers from the posterior canal and the saccular macula form the inferior vestibular nerve.

The position of the vestibular afferents changes as the vestibular nerve approaches the brain. Fibers from the SSC's are situated at the anterior portion of the vestibular nerve, while the saccular and the utricular branches come together at the ventroposterior margin of the vestibular nerve. This knowledge is important for interpreting clincovestibular tests. For example, caloric tests and rotatory tests evaluate the horizontal SCC and thus the superior division of the vestibular nerve, whereas the colic vestibular evoked myogenic potential (cVEMP) test evaluates the saccule and thus the inferior vestibular branch.

The vestibular primary efferents project into the vestibular nuclear complex in the pontomedullary region of the brainstem and the cerebellum, with the highest projection to the nodulus and uvula.

Vestibular nuclear complex:

In the brain stem reside four classic vestibular nuclei. they include:

Superior vestibular nucleus

Lateral vestibular nucleus

Medial vestibular nucleus

Descending vestibular nucleus

In addition to these four nuclei, there are several small groups lying at the periphery of this vestibular complex receiving vestibular primary afferents. These include:

y-group

Interstitial nucleus of the vestibular nerve (INT8)

Parasolitory nucleus (Psol)

Nucleus Intercalatus

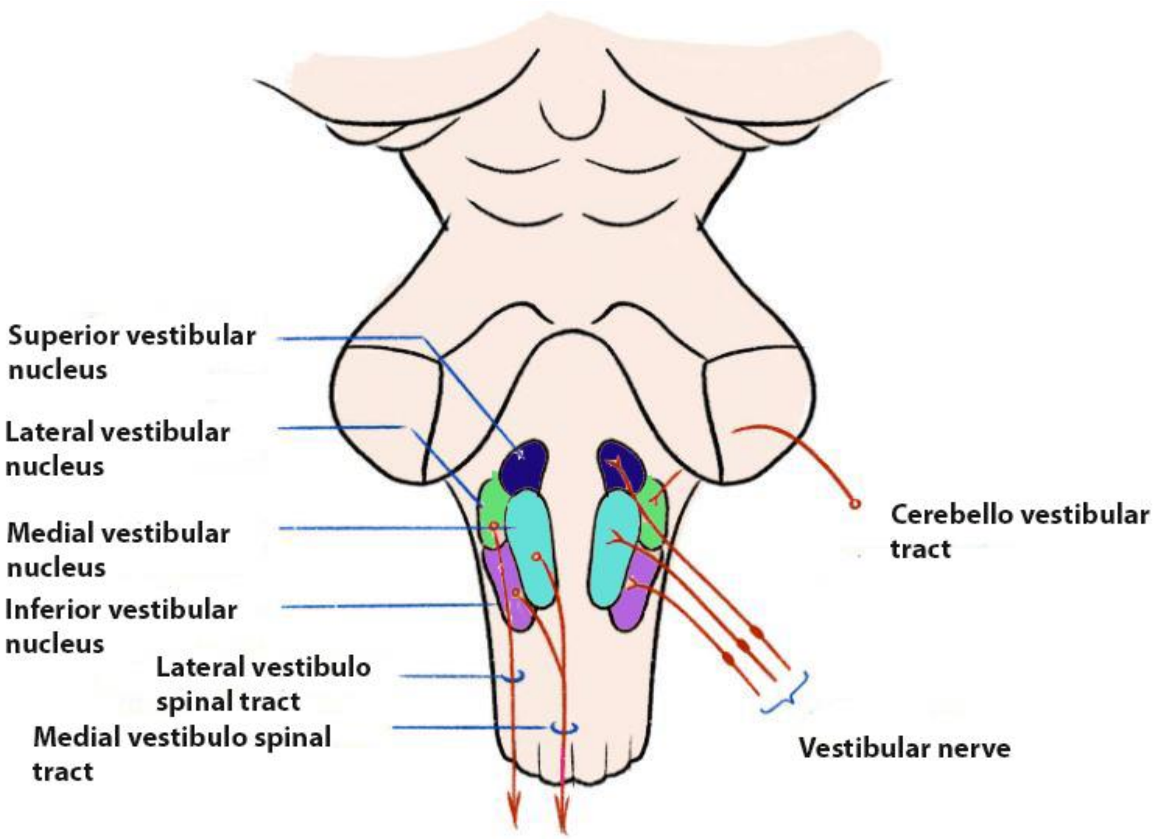


Image showing vestibular nuclear complex

Afferents from SCC's and otoliths enter the vestibular nuclear complex at the level of the lateral vestibular nucleus and rostral descending vestibular nucleus. Then they divide into ascending and descending pathways. The ascending pathway mainly projects into the Superior vestibular nerve and further on to the cerebellum. The descending branch innervates the central region of the vestibular nuclear complex.

Topography exists within the vestibular complex, but it is not well defined. There is a huge confusion among researchers on this topic. Some of the accepted facts pertaining to this topic are:

1. SCC's project to all four vestibular nuclei with the heaviest projection to the Medial vestibular nerve and Superior vestibular nerve

2. Saccular afferents project strongly to the Dorsal vestibular nerve, the INT8 and the Y-group and weakly to other vestibular nuclei

3. Utricle mainly projects to the lateral and dorsal portions of the Medial vestibular nerve, the ventral and lateral portions of the Superior vestibular nerve and the rostral portion of the Dorsal vestibular nerve.

Afferents from the non-vestibular systems like optokinetic system, the neck proprioceptive system and the cerebellar purkinje cells also project into the vestibular nuclear complex.

Within the vestibular brainstem nuclei there are commissural projections reinforcing the vestibular inputs.

Second order neurons from vestibular nuclear complex project to different pathways. These neurons contribute to the control of balance by influencing the discharge of motor and premotor neurons.

Vestibulo ocular pathways:

The central and dorsal regions of the SVN, the MVN and the ventral part of the LVN, as well as the dorsal division of the y-group project heavily to the oculomotor nuclei by means of the medial longitudinal fascicle and ascending tract of Deiters.

Vestibulo spinal pathways:

Most important of Vestibulo spinal pathways are the lateral vestibulospinal tract and the medial vestibulospinal tract, as well as the lateral and medial reticulospinal tracts. Vestibulo spinal pathways originate from vestibular nuclei complex.

Vestibulocerebellar pathways:

This pathway contains fibers from all parts of the vestibular nuclear complex, and mainly project to the cerebellar flocculus, paraflocculus, nodulus and uvula.

Excitatory pathways:

When head rotates to one side the ampulla of the ipsilateral horizontal canal is stimulated followed by an immediate increase in the firing rate of the neurons which is proportional to the velocity of the head turn. These signals project to the ipsilateral Medial vestibular nucleus. Other parts of the vestibular nucleus are also involved. From these nuclei axons decussate onto the contralateral abducens nucleus which innervate the lateral rectus of the contralateral eye through the 6th nerve nucleus. The interneurons of the contralateral abducens nucleus project through the longitudinal medial fasciculus to the ipsilateral medial rectus sub nucleus in the oculomotor nucleus complex activating the medial rectus muscle of the ipsilateral side. The ipsilateral medial rectus and contralateral lateral rectus contract simultaneously.

Inhibitory pathways:

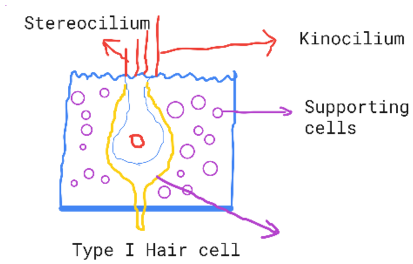
In addition to the contraction of ipsilateral medial rectus and contralateral lateral rectus relaxation of antagonist eye muscles are initiated. This is generated by inhibitory signals from type I neurons in the ipsilateral medial vestibular nucleus.

Vestibular sensory cells:

Vestibular sensory epithelium is formed of hair cells. These hair cells more or less resemble those found in the cochlea also. Two types of hair cells are seen:

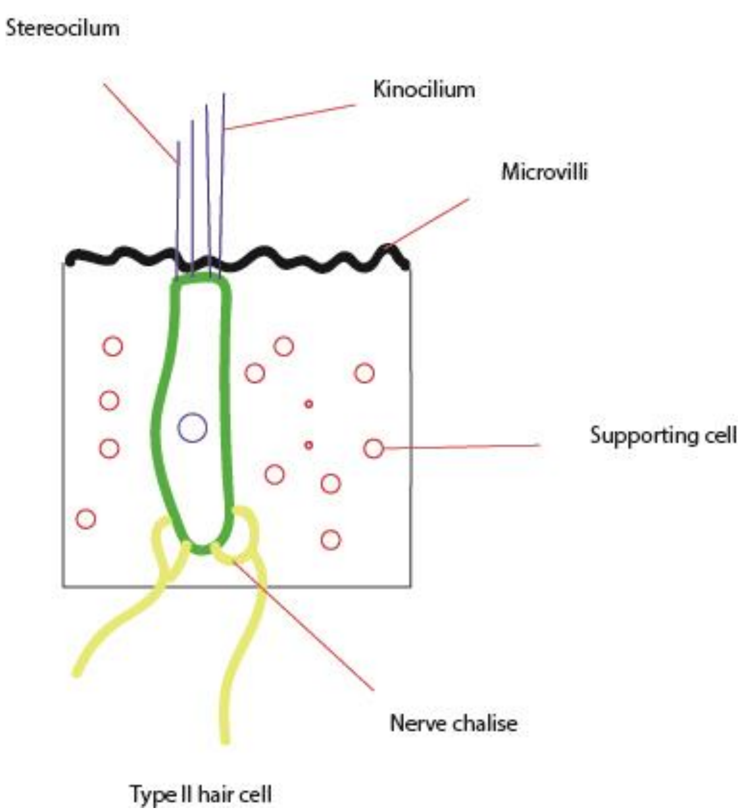
Type I hair cells:

These hair cells are flask shaped with a spherical nucleus. This cell is usually surrounded by chalice like afferent nerve ending. Efferent nerve buds impinge on the afferent nerve chalice.



Type II hair cells:

These cells are cylindrical in shape, with a cylindrical nucleus. It has bud shaped afferent and efferent nerve endings located at the distal end of the cell. The apex of the hair cells is bathed in endolymph and is surrounded by non-sensory supporting cells and dark cells.



The cell's hair bundle serves as the receptor for mechanical stimuli and is located in the apical end of the cell. Each bundle consists of 20-300 stereocilia and a single kinocilium. The stereocilia are rigid tubes of plasma membrane with a cytoskeleton of actin filaments cross linked by fibrin. They are arranged in a hexagonal pattern and vary in length across the surface of the cell, with the shortest stereocilia at one end while the tallest at the other end of the apical membrane adjacent to the kinocilium. The hair bundle resembles a staircase. The ion channels involved in mechanoelectrical transduction are located in the stereocilia and each stereocilium possesses only one or few transduction channels.

Stereocilia are connected to each other by tip links. These are fibrillary strands running obliquely from the distal end of one stereocilium to the side of the longest adjacent stereocilium. These links are connected to the molecular gate of transduction channels. The kinocilium is located at the tall edge of the bundle. The kinocilium is a true cilium consisting of an axoneme. The role of the kinocilium is to transmit the stimulus forces to the stereocilia.

Hair cells are organized differently depending on the location in the SCC's or the otolith organs. Hair cells in the SCC's are located at the crista ampullaris, which is an elevated sensory area within the ampulla of the SCC. The tips of the cilia are embedded in a gelatinous cupula attached to the membranous labyrinth and functions like a diaphragm.

Hair cells in the horizontal canal are excited by flow of endolymph towards the utricle (utriculopetal), while hair cells in the vertical canals are excited by endolymph flow in the opposite direction (utriculofugal). This arrangement forms the basis of Ewald's first law which states that the head and eye movements always take place in the plane of the canal being stimulated in the direction of the endolymph flow.

Ewald's laws:

First law: Stimulation of semicircular canal causes movement of the eyes in the plane of the stimulated canal.

Second law: In the horizontal canals an ampullopetal endolymphatic movement causes a greater stimulation than an ampullofugal one

Third law: In the vertical canals the reverse is true.

In the utricle and saccule hair cells are located in a structure known as the macula. The utricular macula lies in the floor of the utricle and the saccular macula is usually present in the vertical plane on the floor of the saccule. The hair cells of the utricle and saccule are embedded in a gelatinous layer impregnated with calcium carbonate crystals known as the otoliths or otoconia.

Mechanotransduction:

This is the principle of functioning of vestibular apparatus. Hair cells can be described as a biological strain gauge. The biological strain gauge principle works thus:

Mechanical stimulation opens up ion channels in the cell membrane. These ion channels are transduction channels. Displacement of the stereocilia towards the kinocilium stretches the tip links increasing the ion permeability of the channel resulting in an influx of cations (mainly potassium and calcium) thus depolarizing the hair cell. Displacement of the stereocilia away from the kinocilium shortens the tip links. This causes closure of the transduction channels and hyperpolarization of the cell. In a steady state condition 10-20% of the transduction channels are open. Hair cell bundle displacement in the positive direction opens transduction channels. Channel opening decreases the stiffness of the hair bundle, which in turn promotes further movement in a positive direction resulting in a positive feedback mechanism. This mechanism is known as "gating compliance".

Adaptation:

This feature prevents saturation of the mechanotransductor response from large and sustained stimuli (longer than 25 ms). During adaptation the transducer's sensitivity is maintained but the position at which the hair bundle displays maximal sensitivity changes from the resting position towards that at which the bundle is displaced with sustained stimulation. The stimulus/response relationship of the hair cells shifts in the direction of the applied stimulus and causes a return of the channel open probability to its resting value. If a second stimulus is imposed during the adaptation stage, the cell responds again.

The purpose of adaptation includes:

1. It avoids saturation of hair cell responsiveness by large / sustained stimuli

2. It allows a cell to detect small stimuli in the presence of enormous background input

3. It places the hair cell bundle in a sensitive region of its operating domain

4. It contributes to high pass filtering because hair cells with very fast adaptation responses are insensitive to low frequency stimuli. Cells in the same receptor organ may have different adaptation responses accounting for differences in frequency responsiveness