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Pharmacology

The vestibular system is a complex set of structures and neural pathways that serves a wide variety of functions that contribute to our sense of proprioception and equilibrium. These functions include the sensation of orientation and acceleration of the head in any direction with associated compensation in eye movement and posture. These reflexes are referred to as the vestibuloocular and vestibulospinal reflexes, respectively. The centrally located vestibular system involves neural pathways in the brain that respond to afferent input from the peripheral vestibular system in the inner ear and provide efferent signals that make these reflexes possible. Current data suggest that the vestibular system also plays a role in consciousness, and dysfunctions of the system can cause cognitive deficits related to spatial memory, learning, and navigation.

Cellular

There are vast amounts of both afferent and efferent cellular connections involved in the vestibular system. Most of the afferent nerve signals come from the peripheral vestibular system found in the inner ear within the petrous temporal bone. The inner ear contains a bony labyrinth and a membranous labyrinth. The bony labyrinth is filled with a fluid known as "perilymph" which is comparable to cerebrospinal fluid and drains into the subarachnoid space. Suspended within the bony labyrinth is the membranous labyrinth that contains a fluid known as endolymph unique in composition due to its high potassium ion concentration. Endolymph within the membranous labyrinth surrounds the sensory epithelium and interacts with hair cells within the vestibular apparatus to cause nerve transmission.

The vestibular apparatus is comprised of the utricle, saccule, and superior, posterior, and lateral semicircular ducts. The sensory neuroepithelium in the utricle and saccule is the macula, and the sensory neuroepithelium in the semicircular ducts is the crista ampullaris. Both neuroepithelial structures contain specialized mechanoreceptor cells called "hair cells." Hair cells contain a vast number of actin-myosin filaments called stereocilia that are connected at the tips by “tip links.” The stereocilia are organized in rows by length, with the tallest stereocilium connected to an immobile kinocilium. The kinocilium is made of the characteristic 9 + 2 microtubule arrangement.

Hair cells are divided into Type 1 hair cells and Type 2 hair cells. Type 1 hair cells have a high variability of resting discharge while Type 2 hair cells have a low variability of resting discharge. Acceleration of endolymph results in the movement of stereocilia, leading to either depolarization or hyperpolarization depending on the direction of the inertial drag. Movement towards the kinocilium causes potassium ion influx and depolarization that results in afferent neurotransmission to the vestibular ganglion. Also known as the Scarpa ganglion, the vestibular ganglion contains thousands of bipolar neurons that receive sensory input from hair cells within the macula and crista ampullaris. Afferent axons from the vestibular ganglion join to become the vestibular nerve. The vestibular nerve then joins the cochlear nerve to become cranial nerve VIII, the vestibulocochlear nerve. Afferent nerve signals carried by the vestibulocochlear nerve are then interpreted by the central vestibular system within the brain. The central vestibular system unites the peripheral signals from both ascending pathways to elicit eye, head, and body motor responses for control of balance and orientation.

Development

The development of the peripheral vestibular system begins with the formation of the otic placodes from surface ectoderm on the third week. During the fourth week, the otic placodes become the otic pits when they become surrounded by embryonic mesoderm. The otic pits then develop into the otic vesicles. The upper portion of the otic vesicle becomes the vestibular apparatus. As the otic vesicle lengthens, a division occurs between the ventral saccular portion and the dorsal utricular portion. The ventral saccular portion becomes the adult saccule and cochlear duct while the dorsal utricular portion forms the utricle and semicircular canals. Ossification of the system begins at 19 weeks gestation and reaches adult size by 25 weeks except for the internal aperture of the vestibular aqueduct that continues to develop until birth. Hair cells and otoconia develop at seven weeks with differentiation of Type 1 and Type 2 hair cells occurring between 11 and 13 weeks

Function

The vestibular system functions to detect the position and movement of our head in space. This allows for the coordination of eye movements, posture, and equilibrium. The vestibular apparatus found in the inner ear helps to accomplish this task by sending afferent nerve signals from its individual components. The utricle and the saccule are responsible for sensing linear acceleration, gravitational forces, and tilting of the head. The neuroepithelium found in the utricle and saccule is the macula which provides neural feedback about horizontal motion from the utricle and vertical motion from the saccule. Embedded within the macula are small calcium carbonate crystals known as otoliths that assist in hair cell response to the inertial drag of endolymph. Angular acceleration and rotation of the head in various planes are sensed by the three semicircular ducts that are oriented at right angles to one another. Each of the semicircular ducts contains a dilation near the opening to the utricle. This dilation is called the ampulla which contains a neuroepithelial structure called the "crista ampullaris." The crista ampullaris is coated by a gelatinous substance known as the cupula which holds the hair cells in place. Unlike the macula, the crista ampullaris does not contain otoliths.

In addition to the functions associated with the peripheral vestibular system, the central vestibular system allows for processing and interpretation of afferent signals and output of efferent signals. Efferent signals include the vestibuloocular reflex, which allows the eyes to remain fixed on an object while the head is moving. This is accomplished by coordinating movement between both eyes involving the parapontine reticular formation and output to various extraocular eye muscles involving the oculomotor and abducens nerves. The vestibulospinal reflex maintains balance and posture through the coordination of spinal musculature with head movement. Cognitive functions that involve the central vestibular system are based on established neural pathways, although many pathways are still unknown. The known central vestibular connections include the vestibulo-thalamo-cortical tract, dorsal tegmental nucleus to entorhinal cortex tract, and nucleus reticularis pontis oralis to hippocampus tract. These tracts form a series of complex connections that play a functional role in self-motion perception, spatial navigation, spatial memory, and object recognition memory.

Mechanism

The mechanism involved with the function of the peripheral vestibular system involves acceleration of endolymph within the various structures of the vestibular apparatus. Head movement in various directions is responsible for this acceleration that results in stimulation of the stereocilia of hair cells. When the head stops accelerating, hair cells return to their baseline position which allows them to respond to further changes in endolymph acceleration. Depending on the direction of acceleration, the inertial drag of the endolymph will push the stereocilia either towards or away from the fixed kinocilium. Movement towards the kinocilium results in depolarization of the hair cell and movement away from the kinocilium results in hyperpolarization and an overall reduction in afferent firing rates. Depolarization results in potassium ion channel opening, followed by calcium channel opening. Calcium channel opening results in neurotransmitter release across the synaptic cleft, leading to nerve transmission to the vestibular ganglion. Nerve signals pass through the 20,000 bipolar neurons in the vestibular ganglion and leave along the vestibular nerve. The vestibular nerve joins the cochlear nerve and enters the brainstem at the pontomedullary junction. The primary processor of vestibular signals is the vestibular nucleus complex that extends from the rostral medulla to the caudal pons. Many signals are sent from the vestibular nucleus to either the thalamus, cortex, or cerebellum that help to process and adjust efferent signals to postural or ocular muscles. Of note, the hippocampus plays an important role in spatial memory, including the functions of navigation and orientation.