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How is the vestibular system affected by microgravity, and what implications could this have on elderly patients with ageing-related vestibular dysfunction?

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Introduction

The vestibular system is in the inner ear; it processes information about motion including acceleration, movement and orientation. It helps our body retain balance. Maintaining balance involves continuous interpretation of sensory inputs. This information comes from visual signals from the visual system, touch sensations from the somatosensory system, and vestibular signals from the vestibular system. The somatosensory system is a neuron network that helps perceive touch, temperature, body position and pain. Normal movements and stimuli do not upset our body's equilibrium. However, after spinning around we all experience dizziness. What causes this, and how does the body return to balance? Astronauts experience similar dizziness and disorientation during their first few days in microgravity. (NASA, the Brain In Space)

Acceleration occurs in two forms, linear and angular. One example of linear acceleration is gravity; gravity is an attractive force that acts on all matter; it is a force by which a planet or other body draws objects towards its centre. Gravity keeps all the planets in orbit around the sun and keeps us all drawn to Earth's surface. (NASA Space Place, 2020); bodily systems have developed to detect gravity and allow us to recognize our position relative to Earth since it is always present. Angular acceleration includes rotations. The vestibular apparatus detects acceleration and responds with appropriate motor activities to control our balance. Our perception of locomotion and self-orientation occurs because of a healthy vestibular system – this is subconscious and autonomic.

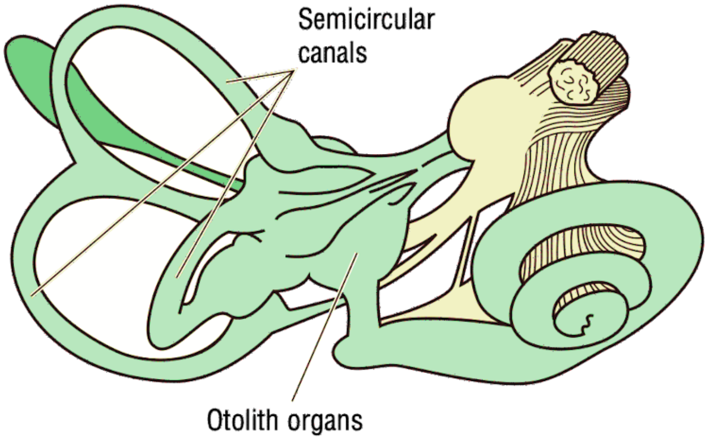
Microgravity likely affects all body systems to some degree, so this review will concentrate primarily on the vestibular system, as it is the organ which detects gravity and controls balance. It will also focus on how the body adapts to attenuate microgravity-induced physiological problems. Understanding the function of the vestibular system will lead to improved adaptation strategies for astronauts entering a microgravity environment and returning to Earth (“NASA - Human Vestibular System in Space”). It will also help aviation pilots, who experience changing gravity levels, and people on Earth, specifically the elderly, prone to dizziness and disorientation.

The impact of ageing on the vestibular system is profound medically and economically. An evaluated \$10-\$20 billion annual expense is associated with fall-related injuries. Data from the National Center for Health Statistics states that 75.3% of the US population over the age of 70 have issues with balance. The number of balance disordered patients due to vestibular dysfunction may reach epidemic proportions. To improve the management of elderly patients with balance disorders, dizziness and vestibular disease, we must research the vestibular system more; expanding this research to the realms of microgravity will offer new perspectives and explanations of the physiology and mechanisms of the vestibular system.

Anatomy and function of the Vestibular System

In the following section, I will describe in detail the anatomy of the vestibular system, as reviewed by Purves D, Augustine Gj, Fitzpatrick D, et al.2001 and Khan 2013 and Brittanica and Kenhub.

The vestibular apparatus is a sense organ located in the inner ear and is responsible for maintaining eye and head positions. Because head mass is constant, detecting head acceleration is equivalent to detecting external forces on the head.



Modified from NASA, the Brain In Space

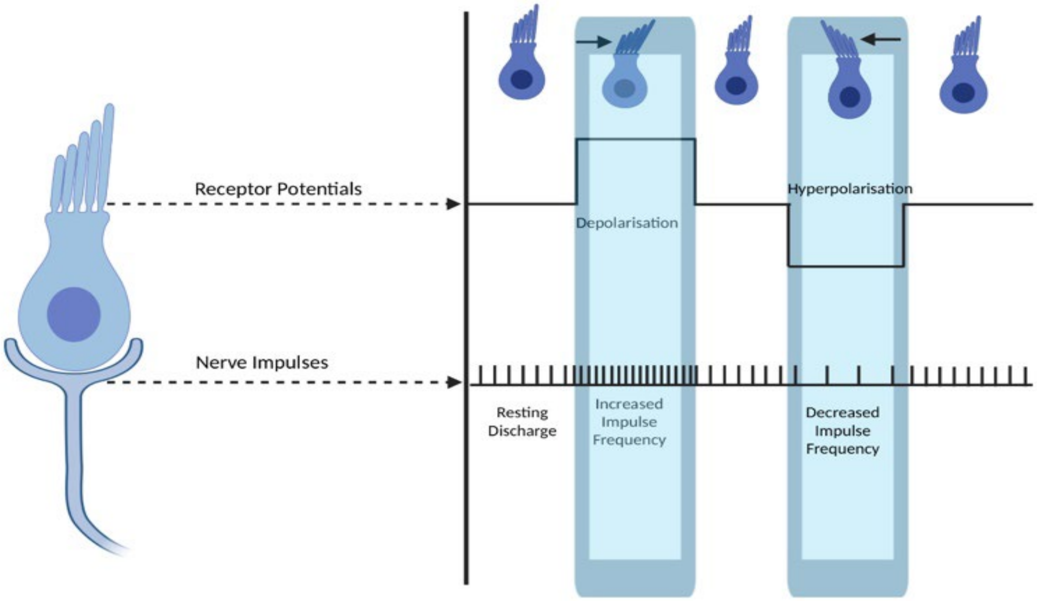
The vestibular system consists of three semicircular canals, two sacs called the otolith organs, vestibular hair cells and other sensory receptors as well as parts of the brain that process vestibular signals.

The cochlea and peripheral vestibular organ make up the inner ear, in the temporal bone. The peripheral vestibular organ consists of the three semicircular canals, the two otolith organs, and the vestibular hair cells. Each of the semicircular canals is perpendicular to one other and detects head movement and acceleration in each plane. The semicircular canals are shaped like tubes, they contain fluid called endolymph fluid and sensory receptor cells called hair cells. Each semicircular canal detects a head movement and acceleration in each plane: nodding up and down, pitch; head tilting towards shoulders, roll; shaking your head as a 'no', yaw. Each semicircular canal has an ampulla which contains crista ampullaris, where the sensory receptor hair cells are. One of the semicircular canals is horizontal and the hair cells are bent most in the yaw axis. Another one is vertical, whose hair cells respond maximally to pitching motions. And the third one is perpendicular to each of the other two and the hair cells are bent most on the roll axis. Semicircular canals also help us to maintain a stable gaze as well as various other important functions.

The two otoliths, the saccule and the utricle have a thicker membrane than the semicircular canals. The hair cells are stuck into a jelly-like membrane, the otolithic membrane. When we move, the otolith sac moves with us. The otolith membrane is filled with otoliths which are calcium stones, commonly known as ‘ear rocks, the otolith membrane and otoliths are denser than the endolymph around it, so the otolith membrane has more inertia than the fluid. So, it weakens during linear acceleration or deceleration of the head, bending and thus stimulating the hair cells. When the head tilts, the sac tilts too, and the weight of the otoliths causes the hair cells to bend. The otoliths detect head tilting and linear motion.

Supporting cells and hair receptor cells comprise the sensory epithelium found in each vestibular apparatus. Stereocilia are on the surface of each hair cell and stick to the other membranes. Vestibular hair cells are the inner ear's sensory receptors, they are the mechanoreceptors. They detect head motion and enable us to orient our bodies and coordinate movements. Vestibular hair cells degenerate with age (Merchant et al. 2000; Rauch SD et al. 2001; Velazquez-Villasenor L, 2000), and drugs also destroy them; what is less well known is that they are affected by altered gravity - microgravity. There are two predominant types, Type I and Type II (Lopez I, 2003). They are both found in central and peripheral portions of the vestibular systems in approximately equal ratios. Type I hair cells, especially the central ones, may be better at detecting acceleration during higher frequency head movements, they respond to more intense vestibular stimulation.

When the head moves, the endolymph fluid within the semicircular canals responds by moving in the opposite direction, as defined by the laws of inertia; the endolymph fluid moves, stimulating the receptor hair cells, which sends an impulse to the brain. The movement of endolymph away from the kinocilium causes the stereocilia on hair cells to move together, closing the cation channels; this lack of potassium influx causes hyperpolarization and inhibits glutamate release. The movement of endolymph towards the kinocilium causes the stereocilia on hair cells to go further apart, opening the cation channels and creating a potassium influx that causes depolarization, and glutamate is released, this triggers action potentials in afferent axons of the vestibular nerve. Glutamate is a neurotransmitter, which means it is a chemical messenger that sends messages between our cells and the brain. Glutamate is important for learning and memory.



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Because vestibular nerve axons continually conduct action potentials to the brain stem and the receptor cells are spontaneously active. So, all the movement of stereocilia does is change the rate of spontaneous activity. Vestibular nerve fibres travel from the inner ear to the brain; they synapse in the brain stem in vestibular nuclei. There are four vestibular nuclei, and they project to the cerebellum, the spinal cord, the neurons controlling the eye and neck and the reticular formation which is a network of brainstem nuclei and neurons that serve as a relay centre for brain processes.

Pathologies related to ageing of the vestibular system

Walking, though it may seem simple, is not simple physiologically; standing upright requires the cooperation of multiple motor and sensory systems, including the vestibular system, visual system, musculoskeletal system, which is the system that supports our weight, maintains our posture and helps us move, somatosensory system and proprioceptive system, a system that provides us with a sense of body awareness (NASA 2009). A compromised performance of any one of these systems can lead to disordered balance. Older people experience more balance impairment compared to others, so considering the rapidly ageing population, dizziness and balance impairment in the elderly may soon reach epidemic proportions. Falling in the elderly and consequent injuries are serious concerns. These are the leading cause of hospital admission and accidental death in the elderly (Zalewski C, 2015).

Out of all these systems, vestibular degeneration is the most common cause of balance impairment in the elderly. Some of the most common vestibular disorders in the elderly include Benign Positional Paroxysmal Vertigo, BPPV, Ménière's disease and vestibular neuritis (Iwasaki et al., 2015).

Vestibular neuritis accounts for around 10% of patients reporting dizziness in otology clinics. The symptoms of vestibular neuritis include long episodes of dizziness and vertigo. The inflammation of the balance sector of the eighth cranial nerve due to a viral infection causes it.

BPPV is the most frequent cause of vertigo in humans (Birla Hospital.); it is more prevalent in the elderly because of degenerative changes to the vestibular system and age, osteoporosis and osteopenia increasing susceptibility. Symptoms of BPPV include short episodes of dizziness and vertigo, usually triggered by a change in head position (Iwasaki S, Yamasoba T. 2015). BPPV seems to be a mechanical problem of the vestibular system; it is believed that it is caused by otoconia in the utricle becoming dislodged and thus going into the semicircular ducts, where they should not be. Over time the otoconia accumulate and interfere with normal endolymph movement, which sends false signals to the brain.

Ménière's disease affects almost 1 in 5 adults between the ages of 60 and 70. The symptoms of Ménière's disease include frequent episodes of vertigo (lasting over 20 minutes), tinnitus (a disorder where you constantly hear a sound not coming from any external cause) and changing hearing levels in the affected ear. It is believed that the leading cause is an overproduction or under absorption of endolymph (Iwasaki S, Yamasoba T. 2015) or a surplus of potassium in an area of the inner ear where it does not belong. This could be due to breaks in the membrane separating the perilymph and endolymph (Haybach and the Vestibular Disorders Association).

Observations of age-related degeneration are in nearly every type of vestibular-related cell and neuron bundle: Including the nerve fibres, sensory end organ hair cells, Scarpa ganglion cells, vestibular nucleus neurons, and Purkinje cells in the cerebellum. Neuron and hair cell loss are some of the most prominent effects of ageing on the peripheral vestibular system. Several studies have shown that ageing reduces the number of sensory hair cells in the vestibular end organs (Johnsson LG 1971) (Engstrom et al. 1974). The beginning of vestibular hair cell decline is usually around the ages of 60-70. A study of temporal bone change from birth to the age of 100 has shown that Type I hair cells from the crista are lost at a significantly larger rate than from the Macula (Rauch et al. 2001). Multiple studies have also shown degeneration of the vestibular ganglion and nerve. Whilst cell decline has been identified, no studies have identified a physiologic reason for this decline – studying the effects of microgravity on astronauts' vestibular system may be able to answer this question.

VEMPs (Vestibular-evoked myogenic potentials) are short-term potentials released by specific muscles in response to vestibular stimulation. They have been used to study the effect of ageing on otolith function (Su HC 2004). The muscle measured affects vestibular nerve function and the inferior oblique muscle of the eye, which measures vestibular nerve function (Lacquaniti, F, 2013). Reduction in the amplitude of VEMPs indicates reduced otolith function, whilst increased amplitude of VEMPS indicates slowed brainstem signal processing (Brantberg 2007). A reduced amplitude of VEMPs has been recognized, implying that there is reduced otolith function in the elderly.

Ageing also relates to a reduction in otoconia mass and fragmentation. This affects the utricle more than the saccule. Currently, the implications of otoconia degeneration on otolith function are unknown, but they may play a role in BPPV. (Johnsson et al. 1972)

Semicircular canals are affected by an age-related decline of the vestibular system. Semicircular canal function is more affected than otolith function. Semicircular canal function has been recorded by studying the VOR (Vestibule-ocular reflex) using caloric testing, which is a vestibular function test. Carol et al. analysed 109 participants and found that the VOR remained stable from the ages of 26 to 79; from then, it significantly declined. A decline in semicircular canal function plays a significant role in the age-related vestibular decline, with a higher prevalence and severity than age-related otolith decline. Given that the semicircular canals measure angular acceleration, it could be that this decline is more associated with the patient's reported dizziness, which poses a risk of falls (Agrawal et al. 2001-2004).

Whilst vestibular decline contributes to balance impairment in the elderly, balance can be affected by many other diseases too. For example, Cataracts, which is a condition where the eye lens' get clouded, affects the visual system and in turn, causes balance impairment. A sedentary lifestyle and arthritis can compromise strength and mobility and significantly impair balance (Vestibular disorder association).

Gravity, Microgravity and Spaceflight

One might believe that gravity does not exist in space. However, because orbital altitudes of human space flight are only around 120-360 miles above Earth's surface, the gravitational field is still relatively strong in these regions. Therefore, orbiting spacecraft stay in orbit around Earth.

Normal gravity, 1g, is the acceleration of an object towards the ground caused by gravity alone near the surface of the Earth (What is Microgravity? NASA). Although there are places of stronger and weaker gravity on Earth, this is the average amount of acceleration. On Earth, if you were to drop an object, it falls at 1g. Whilst if an astronaut in space were to drop an object, it would still fall, but it does not look like it is falling. This is because the spacecraft, the astronaut and the object are all falling at the same rate, so they appear to float in a state of microgravity, 0g (May 2017).

Objects in orbit or free fall are weightless. One can likely experience weightlessness on Earth. Lots of amusement parks have rides that have brief periods of free fall. In addition, skydiving or bungee jumping also frequently incorporates periods of weightlessness.

Astronauts who spend time on the International Space Station or in orbit all experience microgravity conditions. It is crucial to study the effects that microgravity has so that we can prepare astronauts for long-term spaceflight to Mars and beyond. (Gilbert, 2020).

Gravity and the vestibular system

Introduction

Gravity is inherent to Earth, so our balance and spatial orientation on Earth depend on gravity. The vestibular organ detects acceleration changes and converts them into neural signals, which are sent to the central nervous system to regulate physiological functions, this includes sympathetic nerve activity (vestibulo-sympathetic reflex)(Yates BJ et al. 2014 and Gotoh TM et al. 2004, and Ray CA, 2000), arterial pressure (vestibulo-cardiovascular reflex), body stability (vestibulo-spinal reflex) (Reschke, 1998), ocular movements (vestibulo-ocular reflex)(Clarke AH, 1998 and Hallgren E et al. 2016), food intake (Abe C, Iwata C, Moria H, 2010), body temperature (Gotoh TM 2004 and Abe C, 2011; Tanaka K et al. 2009; Abe C et al. 2011) and muscle and bone metabolism (Vignaux G, 2013).

Given that the vestibular system is highly plastic, which means that its sensitivity is altered depending on the gravitational environment, and has so many functions, the plastic alteration of the vestibular system may play a role in microgravity-associated medical issues; for example, space motion sickness and orthostatic hypotension, which is a condition where a person experiences a sudden decrease in blood pressure when standing up (Moria et al., 2020). Because the vestibular system has so many roles, its ability to adjust to each of these reflexes will change when it goes through plastic alteration. For example, Hallgren et al. determined a correlation between decreased otolith function and orthostatic hypotension. This suggests that the plastic alteration of the vestibular system in terms of cardiovascular wellbeing was ineffective. Each reflex will have different responses to this plastic alteration, so it disrupts many vital functions.

The brain's internal model of gravity

Gravity produces disequilibrium torques which affect movement, so we believe our brain has an internal model that anticipates sensory consequences of our actions in gravity. A torque is a vector quantity; if the size of the torques acting on the objects is balanced, and the directions cancel each other out, the object is in equilibrium. But in the case of the earth, gravity causes a net resultant force on the body, so the body is not in equilibrium anymore. This internal model will likely maintain our posture, spatial orientation and precise voluntary movement by comparing vestibular signals with information from proprioceptive, somatosensory and visual systems with the brain's internal models' predictions (Wolpert et al., 1998; Wolpert and Ghahramani, 2000).

Sensory systems often provide ambivalent information; the brain must have neural processes to resolve these ambiguities. For example, when the head moves in gravity, the otoliths shift with the direction of gravitational acceleration so that the hair cell receptors move and signal the brain of gravity (Gallagher et al., 2021). Nevertheless, it cannot distinguish between linear acceleration and gravity. It is believed that the brain uses internal models, defined as “a neural mechanism that imitates the movement of an object to help with sensory, motor and cognitive functioning" (Zago, Lacquaniti, 2005)) to distinguish between linear acceleration and gravity. (Merfield, 1999)

The internal gravity model is a network of subcortical and cortical regions (Gallagher et al., 2021). These parts will have increased activity when seeing targets falling with normal earth gravity versus objects not accelerating according to gravity. The vestibular system connects with the proprioceptive system; many neurons respond to vestibular and proprioceptive inputs. A change in the integrated proprioceptive and vestibular neuron signals may drive the shift in gravity-produced disequilibrium torque (Miller WL et al. 2008); direct evidence for this is still necessary. Because fast interactions between our limbs and the external environment do not happen solely under sensory feedback due to inaccuracies and delays, we know that some mechanism other than the vestibular system is involved (Zago, Lacquaniti 2005). Nevertheless, direct evidence of this internal model is needed, so some people still seem to reject this theory.

Gravity plays a substantial role in perception and behaviour. In human vision, the motion perception is more precise for objects falling with gravity versus objects not moving with gravity. Eye movements are more precise when tracing objects in 'normal' gravitational conditions versus objects in microgravity or hypergravity. In addition, the interception of moving objects is also more accurate in 'normal' gravity; in microgravity, there is a significant impairment in intercepting and predicting moving objects (Gallagher, 2021). Microgravity motor responses were often too early (Zago, Lacquaniti 2005). Together, this suggests that gravitational acceleration is considered when we interact with our world, most likely through neural systems; this indicates that the internal model of gravity exists. (Gallagher, 2021). In addition, humans show asymmetric arm movement; this means that they are probably responding to marginally different environmental conditions, suggesting that the brain's internal model of gravity controls it (Gaveau et al., 2016).

Since we are constantly in a terrestrial gravity environment, it seems likely that an internal model of gravity influences our joint position sense which is defined as knowing where our limbs are in space for more effective interaction with the external world. Joint position sense incorporates muscle spindles, joint mechanoreceptors and the amount of effort required to move. Studies have shown that changes in the disequilibrium torque of limbs, produced by gravitational acceleration, change the joint position sense (Bringoux L, 2011) (Ettinger and Ostrander, 2018). For example, studies had shown that when participants tried to match a target angle when seated upright usually and then with a small weight applied to the arm, an overshoot was reported with the weight; When participants were in the water, an undershoot was produced instead - basically due to the reduced gravitational torque acting on the arm. On the other hand, the target angle was matched normally again on the application of an additional torque in microgravity conditions. This supports the conclusion that an internal model of gravity exists.

This internal model of gravity can be innate, or it can be learnt, which is a vital feature for astronauts adapting to microgravity (Sago, McIntyre 2008). How long it takes to learn a new model or adapt to an existing one also depends on the environment. Natural selection will favour adaptation to a biologically relevant property of the environment which usually applies to properties that hold throughout habitable environments; gravitational acceleration is the perfect example.

Readjusting to Earth's gravity impacts astronauts' balance since the brain's internal model must readapt to interpret the sensory input in normal gravity versus microgravity. While acclimatizing, astronauts experience motion sickness symptoms including headaches, and perception issues (NASA 2009).

Interaction of the vestibular system and the musculoskeletal system

Our motor systems have neural mechanisms to stabilize our posture and overcome the force of gravity, it is worth noting that these neural mechanisms remain functional when first exposed to microgravity (Goldberg et al., 2012). Motor neurons carry signals from the brain via the spinal cord; they sit close to muscle fibres and release chemicals which make the muscles contract. Since we constantly overcome the downward force of gravity on Earth, our muscles are continually working. However, in space, microgravity has been shown to induce muscle wasting. Since the muscles are damaged, they either then cannot receive messages from the neurons, or they cannot respond to them (Sivadas, Broadie 2020). This may be partly due to vestibular dysfunction.

Gravity change can alter the vestibular system, which links the sympathetic and motor nervous systems; these are crucial to regulating muscle and bone metabolism. The sympathetic nervous system controls the involuntary responses to stressful/dangerous situations. Evidence for this is from a study that performed labyrinthectomy on rodents. A labyrinthectomy is a surgical procedure that removes parts of the vestibule and semicircular canals; this is usually performed to treat vertigo if you have little hearing in the suffering ear. Reports of Reduced bone mass after the labyrinthectomy indicates that the vestibular system may regulate bone metabolism (Vignaux et al., 2013; Vignaux et al., 2015; Levasseur et al., 2004). Labyrinthectomy induces changes in the structure and function of muscle fibres in rodents. The vestibular system also has a particular role in modulating muscle fibre size and transcription factor (Luxa et al. 2013 and Shall MS et al. 2005) expression in rats. Transcription factor expression is what controls gene expression. Other clinical studies have reported a relationship between BPPV, vestibular dysfunction, and osteoporosis. Together, these findings indicate that the vestibular system plays a particular role in skeletal muscle and bone metabolism.

Microgravity-induced muscle wastage in astronauts recovers faster than osteopenia, which is low bone density usually experienced by the elderly (Kawao N et al., 2018). This suggests that gravity change may influence the musculoskeletal system by affecting myokines, proteins made and released during muscular connections. If we turn to hypergravity conditions for a moment, a DNA analysis of mouse anti-gravity muscles has shown that the gene for a protein (FKBP5) is responsible for the hyper gravity-induced muscle mass increase through the vestibular system (Shimoide T et al. 2018). Several myokines secreted from the skeletal muscles affect bones (Kaji H, 2016) and could be involved in how gravity changes muscles and bones through the vestibular system. Follistatin is a binding protein that can increase muscle mass and strength. Hypergravity enhances follistatin expression in the anti-gravity muscles and the following secretion to the bloodstream through the vestibular system in mice (Kaji H, 2016). If the opposite occurs in microgravity, then maybe inhibiting the expression of the protein will be a treatment option for preventing muscle wastage from osteopenia or microgravity.

In conclusion, it seems likely that vestibular system plasticity could be crucial for understanding the effects of microgravity on the musculoskeletal system. More research is required on Follistatin and FKBP5 expression in altered gravity conditions to find how this can be applied as a treatment for the elderly with osteopenia and astronauts suffering from muscle wastage.

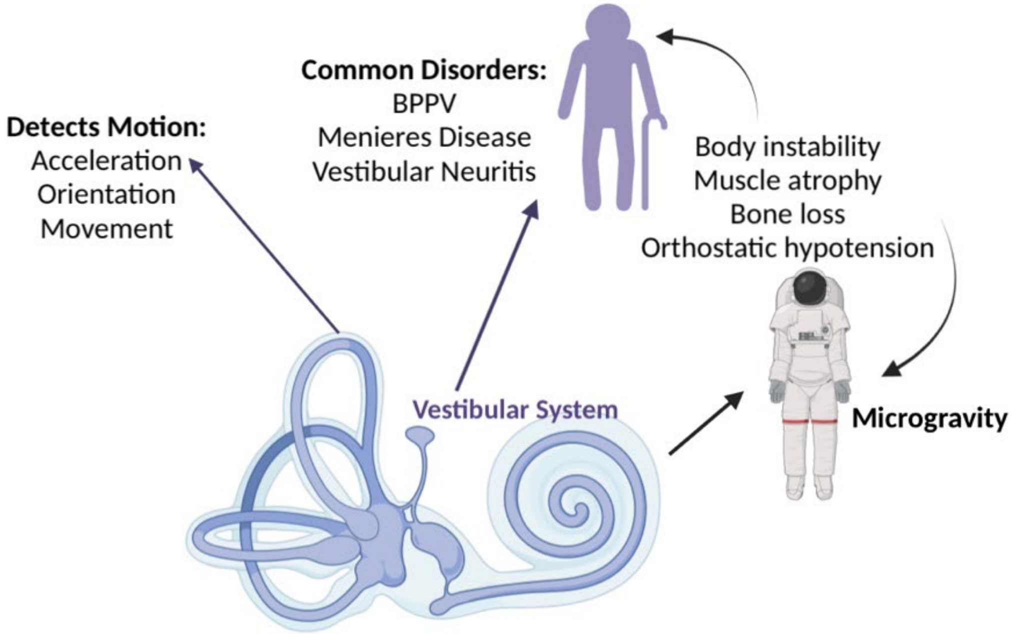
Interaction of the vestibular system and the cardiovascular system

When we go from lying down to standing, the hydrostatic pressure, which is pressure due to fluids, on the lower body increases, and the blood builds up in the lower body (Robertson, 2008). There is a reduction of blood volume in the thorax and a reduction in heart filling, cardiac output and arterial pressure; the circulatory control mechanism quickly corrects these changes, so it does not result in a decreased arterial pressure in healthy people.

Arterial pressure in posture changes is maintained by the baroreflex, a mechanism to maintain blood pressure, and the vestibulo-cardiovascular reflex (Abe C et al. 2011). The gravity change that goes with a posture change causes a downward blood shift and a decrease in arterial pressure. This gravity change triggers the vestibular system and increases arterial pressure.

Around a third of older adults have orthostatic hypotension (Salminen et al. 2012), and so do nearly half of the astronauts who return from a space mission (Mech JV et al. 2004). Among other mechanisms, animal studies comparing the arterial pressure response to posture changes in animals with a healthy vestibular system and animals with vestibular impairment have shown an involvement of vestibular system dysfunction in orthostatic hypotension (Morita et al 2016 and Abe et al. 2008 and Tanaka et al. 2012).

In astronauts, the plastic alterations of the vestibular system reduce the ability to adjust and adapt the vestibulo-cardiovascular reflex. Recently a significant correlation between decreased otolith function and reduced arterial pressure response upon returning from spaceflight has been found; this suggests that decreased otolith function may cause orthostatic intolerance (Hallgren et al., 2015). Furthermore, as otolith function readapted to gravity on Earth, the vestibulo-cardiovascular reflex gradually recovered; the effect is not permanent. In addition, a reduction in the ocular counter-rolling response, which is vital for stabilizing gaze, has been reported upon return from long-term spaceflight (Hallgren et al. 2016).



What happens to the vestibular system in microgravity

Introduction

Acute exposure to microgravity and altering gravity challenges the integration of neuro-vestibular signaling. This challenge is associated with space motion sickness and alterations in spatial abilities, which is the ability to remember objects in space, and sensorimotor function, which is maintaining equilibrium in joints during body movements (Reschke and Clément 2018).

In microgravity, head tilting does not stimulate the otoliths. This alters the sensory input from the vestibular system, which generates a conflict between expected sensory input from the brain's internal model of gravity and actual sensory vestibular inputs. Conflicting information from semicircular canal signals and visual signals during movement are also seen.

A good example is if you were to do a cartwheel in microgravity, the input from your semicircular canals and vision would be identical to that on Earth. However, the input from the otolith organs would be inconsistent because it would not signal that the direction "up", against gravity, changed. This inconsistent sensory input is regular in microgravity.

Usually, the signals from all these sensory systems are consistent with each other. However, inconsistent sensory input can lead to motion sickness and illusory perceptions in microgravity. This renders them unable to differentiate up and down. This theory is known as the sensory conflict theory.

Type I and Type II vestibular hair cells are affected by microgravity. Prolonged stay in a microgravity environment predominantly affects the structure of type II hair cells (Ross, 2000). Structural analysis has shown an increase in type II utricular hair cell synapse in mice after a 9-day space flight (Ross, 1994). After two weeks, increasing numbers of type I cells were also observed. However, after 15 days in microgravity, there was a reduction in the synapse densities of hair cells in the mouse utricular hair cells (Sultiemeier et al. 2017). These changes are likely to affect and contribute to the symptoms experienced by astronauts during space flight and post-return to Earth (Carriot, 2021).

Microgravity also affects the vestibular afferent nerves; hair cells transmit sensory information to afferent neurons; initially, in microgravity, the sensitivity of the otolith afferents and the baseline activities of the otoliths increase (Clement et al., 2020). Then around five days later, they seem to return to normal levels. (Bracchi et al., 1975). The hypersensitivity of otolith afferents induced by microgravity may be due to a presynaptic adjustment of the synaptic strength in hair cells (Ross, 2000). However, space missions that have further investigated this have reported contradictory results. Given this variation, how microgravity influences the responses of vestibular afferents in mammals remains unclear (Cullen and Wei, 2021).

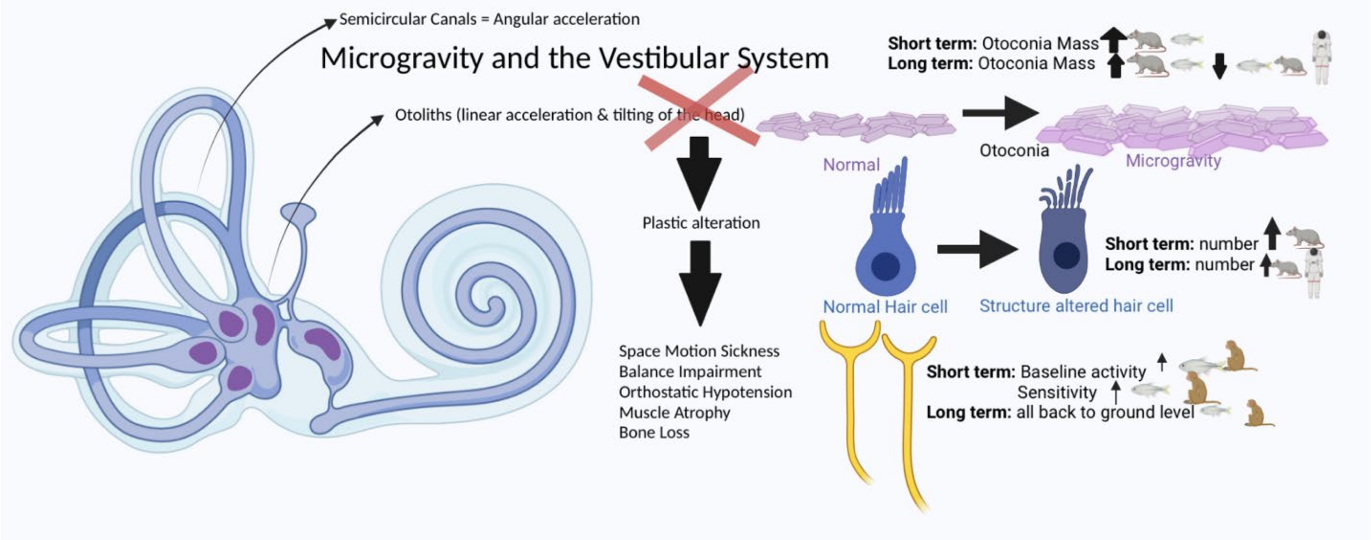
Projections of the vestibular pathways to the limbic system and neocortex are important for brain plasticity, which includes memory formation and spatial learning (Smith 2017). Peripheral lesions of the vestibular pathways link to atrophy in the hippocampus and possibly permanently impaired spatial learning (Smith et al., 2010).

Neurolab scientists are studying why astronauts feel unsteady on their feet and experience balance difficulties on return to Earth. The somatic sensory system which processes signals from vestibular, visual, tactile and proprioceptive systems, which play a large part in balance, has been studied. One experiment correlated eye movement with spatial orientation, suggesting that eye movement plays a significant role in spatial orientation. Studies on Earth have also shown that movements of the eyes reveal what is happening in the inner ear. Therefore, astronauts maintain spatial orientation in space without the known "down" direction that gravity provides on Earth by depending heavily on vision or external reference points.

Experiments such as the ball catching test see how the perception of moving objects change in microgravity, the use of a virtual environment system to study body orientation and a study of the effects of microgravity on pointing and reaching tasks. Data collected from these experiments provide insight into how the nervous system creates a balance between information gathered from the eyes, inner ears and joints.

Some of the long-term effects of microgravity include an alteration of the electrocortical function and structure of the cerebellum, which is responsible for coordination and motor control. Altered peripheral input may affect vestibular nuclei and cortical projections which is where the integration of sensory inputs occurs. Furthermore, the frequent observations of impaired voluntary movement in experienced space crew suggest changes in the structure and function of the cerebellum (Van Ombergen 2017).

If we look at hypergravity conditions for a moment, studying behaviors reflecting the function of the otolith organs in the rat has found that following chronic hyper-gravity exposure has considerably altered their function too. In hypergravity conditions, there has again been a reduction in synapse densities of otolithic hair cells. These findings suggest that the sensitivity of the otoliths has decreased following chronic hypergravity exposure. Using experimental techniques, the otolith spinal reflex has been studied and has found evidence supporting the conclusion that long-term exposure to hypergravity leads to a decrease in sensitivity of the otoliths (N. Daunton, 1996). This perhaps is evidence supporting that the otoliths become hyposensitive in a microgravity environment.



Following short-term exposure to microgravity, the mass of the otoconia increases. This increase is maintained if there is no other alteration to gravity. After a short-term stay in microgravity, type II vestibular hair cells increase in size and number; after a long-term stay in microgravity, type I vestibular hair cells grow in number too. In hypergravity, hair cells decrease in number. After short-term microgravity exposure, there is an increase in vestibular afferent nerve normal sensitivity and activity. After a while, they return to ground levels. The structure of the cerebellum is also altered after transitioning to microgravity.

Space motion sickness (aka ' gravity sickness')

Space motion sickness is a prevalent clinical condition observed during space missions. It can harm astronaut health and affect the efficiency of space missions; it has many symptoms of terrestrial motion sickness, including headaches, concentration difficulty, loss of appetite, and vomiting. The sensory conflict theory, as described before, and the fluid shift theory are two possible explanations for the neuro-vestibular cause of space motion sickness.

The fluid shift theory is that microgravity affects the normal distribution and composition of body fluids. The body responds through diuresis, which is an increase in the production of urine. This redistribution of fluid is interpreted as an increase in circulating blood volume. So ADH release, which controls the permeability of the walls of the collecting duct in the kidney, is inhibited. The increase in the loss of sodium, potassium and chloride through excretion is reversed on return to normal gravity, as is the total decline in body water and plasma volume. If we assume that endolymph fluid will react in the same way, this change in the makeup and the volume of endolymph might mess up the vestibular response (The Brain in Space NASA). However, this mechanism remains speculative, and no direct flight evidence exists.

Astronauts may even become disorientated due to the inability to detect where their limbs are – this is remarkably like symptoms experienced by the elderly with vestibular function decline.

Space motion sickness and microgravity-induced vestibular dysfunction may consider the Coriolis effect and vection. The Coriolis effect occurs when the head is in motion and constantly changing direction, so acceleration information is bombarding each semicircular canal at once. The vestibular organs connect with the cerebellum, the eyes, and the hypothalamus, which controls several autonomic functions and others. As a result of the overstimulation, these connections are responsible for nausea and dizziness. Vection is the illusion that the body is moving in a circle or a line when it is not. Visual cues, especially in the periphery of one's vision, affect the sense of movement, even without actual body movement. This connects to ageing, where the vestibular system is declining. Byron K.

Lichtenberg, an astronaut, commented on his spaceflight experiences and said, "I immediately felt as though we had flipped 180 degrees." The otoliths do not perceive a downward pull during head movements; this contributes to the visual orientation illusions and feelings of vertigo and self-inversion.

A change in the gravitational field strength acts as a stressor to the body, and long-term stress induces a body temperature decrease. Short-term gravity changes activate the sympathetic nervous system in rodents and humans (Abe C et al. 2008 and Abe C et al. 2007; Hammam et al. 2012; Hammam et al. 2017). Space motion sickness may induce hypothermia (Markham and Diamond, J. Vest. Res., 1993).

Since reports of otoconia deletion suppress hypergravity-induced hypothermia, the vestibular system seems involved in space motion sickness-induced hypothermia. The people experiencing nausea during caloric ear stimulation showed an increased sweating rate on the forehead (Cui J et al. 1999). This perhaps is evidence of the relation between vestibular dysfunction and hypothermia.

Symptoms associated with an age-related decline of the vestibular system are comparable to those associated with being in a microgravity environment. How can insights from microgravity studies help us further understand the susceptibility of the elderly to balance impairment?

Barry W. Peterson and researchers, supported by NASA and the NIH, are creating the first whole-body computer model of human posture and balance control to connect this work with patients suffering from balance disorders.

Comparison between the vestibular system in microgravity and ageing-related vestibular dysfunction

Microgravity-induced plastic alteration of the vestibular system can cause symptoms of body instability, muscle atrophy, bone loss and orthostatic hypotension (Hironobu et al., 2016).

It is well known that as we age, the risks associated with falling become greater, implying that ageing causes increased body instability; ageing involves an involuntary loss of muscle mass, this is called sarcopenia; after the age of 50, people tend to start losing bone mass too, commonly known as osteoporosis; finally, orthostatic hypotension is frequent in the elderly. Why is it that the symptoms of microgravity-induced plastic alterations of the vestibular system present similar symptoms to those that the elderly experience? It suggests a common factor in the change of the vestibular system.

By 75 years of age, people have usually lost up to 60% of their vestibular hair cells (Zalewski, 2015); as discussed before, astronauts who experience a prolonged stay in a microgravity environment seem to have an altered structure of type II hair cells and a reduction in the synapse densities of all hair cells (Sultiemeier et al. 2017). These changes are likely to affect the elderly and contribute to the symptoms experienced by astronauts during space flight and post-return to Earth. (Carriot, 2021)

As discussed before, the dislodging of otoconia into the semicircular ducts causes BPPV. The elderly are more prone to this. Endolymph fluid does not usually react to gravitational conditions. However, the otoconia do, so they move the endolymph even when it is usually still. When the endolymph moves, the hair cells are stimulated and send messages to the brain that the head is moving, even though it is not. The conflicting information of this with the eyes, muscles and joints is what seems to cause BPPV in the elderly and causes a spinning sensation, vertigo, which will usually last for a few minutes (Vestibular disorders association). Astronauts can experience this vertigo during space motion sickness; maybe studying countermeasures for this will help the elderly prone to BPPV.

Terrestrial motion sickness is a sickness associated with travelling on Earth. Elderly people are more prone to motion sickness than others, this may be because of a degenerated otolith system. This may explain why astronauts are so prone to space motion sickness.

It is worth mentioning that astronauts in space are more prone to cataracts due to the acute exposure to the radiation they experience in space; this will affect their balance too. The fluid shift in microgravity induces glaucoma, which is an increased pressure in the eye which damages the optic nerve that connects the eye and the brain, in astronauts, affecting astronauts' balance too. Studies have found eye structure and vision abnormalities in all the astronauts studied. The most usual ones include changes in the retina and the optic nerve; these changes seem to persist long after their return to Earth (NASA 2013). Vision changes severely impact their balance, which will contribute to the loss of balance they experience on return to Earth. The elderly is also more prone to these eye conditions, so another common factor has been found which may induce balance issues.

During the 1960s, NASA sponsored a Man Vehicle Laboratory at MIT to study the effects of long-term space flight on astronauts. One of the studies involved research on human movement and balance, led by Lewis Nashner and supervised by Dr Larry Young. Their work has resulted in CDP (Computerized Dynamic Posturography), a non-invasive technique that assesses the systems involved in balance using protocols to assess impaired balance function. CDP is now valid for studying astronauts' impaired balance and those suffering from balance impairment, usually the elderly. CDP is now the standard medical tool for testing impaired balance.

Through working with NeuroCom, there are now several methods for testing for balance impairment, of which the dynamic models involve a patient standing on the systems platform, the platform shifts and measures the forces applied by the feet as the patient attempts to stay balanced. The patient is also tilted to test the visual component of the patient's balance mechanisms. This system can identify patients' sensory and motor impairments and compare them to the average values experienced by patients in the same age range. After identifying the problem, it is easier to help the patient learn and perform the struggled tasks more quickly and safely.

This technology is estimated to save at least $19 billion annually for the CDC (centre of disease control) to prevent falls in the elderly. "Because NASA has to deal with the complex problems of flying people in space, their research tends to be more applied and closer to what we need to take hold of and put into general medical practice." Said a spokesperson of NeuroCom (Medical Devices Assess, Treat Balance Disorders - NASA, 2009).

This is the perfect example of how researching astronauts in space has helped and provided invaluable research for patients here on Earth suffering from disorders, in this case, the elderly suffering from balance impairment. Whilst we keep drawing parallels between what happens to the astronauts' bodies in space and common physiological problems experienced on Earth, we will keep being able to push the boundaries of medical technology.

Looking to the future

Galvanic vestibular stimulation has prevented hyper gravity-induced plastic changes of the vestibulo-cardiovascular reflex (Abe C et al. 1985 Morita H 2009). If the same occurs in microgravity, incorporating galvanic vestibular stimulation with training in space flight and as a treatment option might be a new countermeasure against vestibular deterioration. More research should be performed to understand how this could be incorporated into astronaut training fully. In addition, a study on whether this can be applied to elderly patients with an impaired vestibulo-cardiovascular reflex should be performed.

So far, there is no documented case of a patient's impaired internal model of gravity. Understanding whether cerebellum structure alterations can cause impairment will be crucial to further understanding how our body functions in gravity and the physiological effects of microgravity. If we find that cerebellum structure alterations can cause an impaired internal model of gravity, this might be a new disorder with symptoms of balance impairment.

The factors through which gravity change and mechanical stress affect muscles and bones seem to differ (Kawao et al., 2018). Further studies are required to understand the underlying mechanisms of microgravity-induced effects on muscles and bones. Controlling the vestibular system and clarifying the critical factors that maintain muscles and bones in response to gravity change might help prevent microgravity or immobilization-induced muscle wasting and osteopenia.

Space motion sickness-induced hypothermia seems to be quite common. The reason remains unclear. Unfortunately, there is no evidence of an evolutionary advantage from this response. Gravity sickness-induced hypothermia is not due to evolutionary pressure; it might be a disturbance created by human technology development. Further research is needed to understand this.

Because a plastic change in the vestibular system alters the vestibulo-cardiovascular reflex, vestibular stimulation may be a treatment for people with cardiovascular disorders such as orthostatic hypotension. Because a plastic change in the vestibular system causes muscle wastage, vestibular stimulation may be a treatment for people with musculoskeletal conditions such as osteopenia. More research should be put into this.

Apart from these, it is essential to research this topic because of how much we can learn that applies to day-to-day problems many of us experience on earth.

To conclude, I have been thinking long and hard about what I want to be the takeaway for this paper, and whilst I think the vestibular system and space research is central, more broadly I want to show that research into space is beneficial. When we are researching space, a lot of what we learn is about Earth; the same goes for the human body, space medicine is allowing us to explore the most extreme adaptations and reactions of our human body and apply this to current medical development. A lot of this research is not aimed at improving our understanding of space, it is aimed at understanding more about us and how we live. We will always be the centre of this research. Researching the vestibular system in space is an intriguing topic because the implications of this research is so close to us, this research will help all elderly who are at risk of falling: our grandparents, great-grandparents, and eventually our parents and us. This research will make a difference.

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