Review Article

Space Physiology and Vestibular Orientation Cues

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ABSTRACT

Space motion sickness caused by an intravestibular conflict, is an important obstacle that astronauts encounter during the initial stay in space.Sensing gravity is critical for perception of spatial orientation, the upright posture, and generation of day to day activities. When an astronaut transitions to microgravity and returns to earth gravity, the vestibular input arising from self-motion does not match the human brain's expectation. Neurophysiological studies provide insight into how the nervous system rapidly reorganizes when evervestibular input is unreliable. However, to date, it is unknown how information regarding rotational and translational components of selfmotion is integrated by vestibular pathways during body motion and momentum.This review may be useful in the workup of vertiginous disorders as well asaltered integration of vestibular and visual cues during interplanetary missions.

Keywords: Saccules,semicircularcanals,space motion sickness, utricles.

INTRODUCTION

Study results showed the presence of muscarinic receptors in the peripheral vestibular system on which scopolamine had a suppressing effect. Given the depressant actions on thesemicircular canals(SCC), it is suggested that the pharmacodynamic effect of scopolamine was the obliteration of intravestibular conflict that arises during space motion sickness (SMS). [1]Nervous system rapidly reorganizes with unreliable changes in vestibular input by both (a) updating its internal model of the sensory consequences of motion and (b) up-weighting more reliable extra-vestibular information. These neural strategies, contribute to improvements in sensorimotor performance like gaze and postural stability, locomotion, orientation and perception, whenever an astronaut enters in to microgravity or returns to earth.[2]Galvanic vestibular stimulation (GVS) adaptation did not occur at the vestibular end-organs involving changes in brainstem-mediated vestibulo- or vestibulo-spinal reflexes. With unreliable patterns of vestibular input, the cerebellum reweighted sensory input to accentuate veridical extra-vestibular informations like somatosensation, vision and visceral stretch receptors, to regain postural function.[3]Hearing and auditory function in crewmembers showed hearing threshold differences between men and women, in which female astronauts showed better hearing thresholds. The researchers were yet to know if increasingly longer-duration space missions cause different neurophysiological responses in men and women.[4]The results of study done by Clément G and Wood S. J., 2014.,suggested that there was a shift in the frequency dynamic of tilt-translation motion perception after adaptation to weightlessness. These findingsgot implications for manual control during landing of a space vehicle after exposure to microgravity in case of human asteroid and Mars missions.[5]Altered gravito-inertial environments diminished vestibular function in controlling balance which triggered increased weighting of fast-adapting (FA) receptors that signal foot contact or slips. Understanding these modulations to skin sensitivity has translational implications for mitigating postural disequilibrium following space flight as well as for on-Earth preventive strategy for imbalance in older adults.[6]For on ground participants, measures of neurocognitive performance, fine motor control, gait, balance, structural MRI (T1, DTI), task fMRI, and functional connectivity MRI were obtained. In flight, astronauts completed pre- and post flight tasks that measuring spatial working memory, sensorimotor adaptation, and fine motor performance. Potential changes over time and associations between cognition, motor-behaviour, and brain structure and function were analysed in the study done by Koppelmans V et al., 2013.[7]Asymmetry between downward and upward pitch turns observed on Earth showed an immediate and significant reduction when free-floating in weightlessness and a delayed reduction when the cosmonauts were firmly in contact with the floor of the space station. The consequence of weightlessness on the early processing stages in vestibular and optokinetics that aid perception of self-motion did not stem from a change in alertness or any other uncontrolled factor in the International Space Station (ISS).Weightlessness had no effect on the perception of yaw turns.[8]For several cosmonauts, until as long as nine days after landing, spontaneous eye movements were increased like spontaneous nystagmus, gaze nystagmus and square wave jerks.Otolith function was suppressed involving inversion, absence, or significant decrease of the compensatory torsional ocular counter-rolling. Vestibular reactivity was elevated with an increased intensity of the vestibular nystagmus during head yaw rotations. Amplitude and velocity characteristics of gaze control were reduced. Total reaction time increased up to 2-3 times and gaze holding ability showed degradation.[9]Astronautswere tested on an obstacle avoidance test called Functional Mobility Test (FMT) and on the Sensory Organization Test using sway-referenced support surface motion with eyes closed (SOT 5) before and six months after space flight on the ISS. Even though higher cut-points increased sensitivity to post-flight astronauts but decreased specificity to pre-flight astronauts.Study findings showed that standard clinical comparisons were not beneficial for identifying problems. Testing both standing and walking balance were better to identify balance deficits.[10]Astronaut showed a heterogeneous response of some increases and decreases in the amplitude of head pitch movement. Body load-sensing somatosensory input centrally modulated vestibular input and adaptively modified vestibular mediated head-movement control during locomotion. The study suggested that, space flight can cause central adaptation of the converging vestibular and body load-sensing somatosensory systems resulting to alterations in head movement control.[11]Impairment in the processing of gravitational input in long-duration space travel affects the mental representation of the vertical dimension in astronauts similar to the otolithic patients. However, the astronauts, recover to baseline levels within seven days after returning to Earth.[12]Meclizine, lorazepamandscopolamine selectively suppressedvarious parts of the vestibular system. This actioncan be more beneficial for alleviating space motion sickness than other general suppressive agents. This indepth analytical knowledge helps the clinicians in their therapeutic management of patients with semicircular canal andotolith dysfunction.[13]

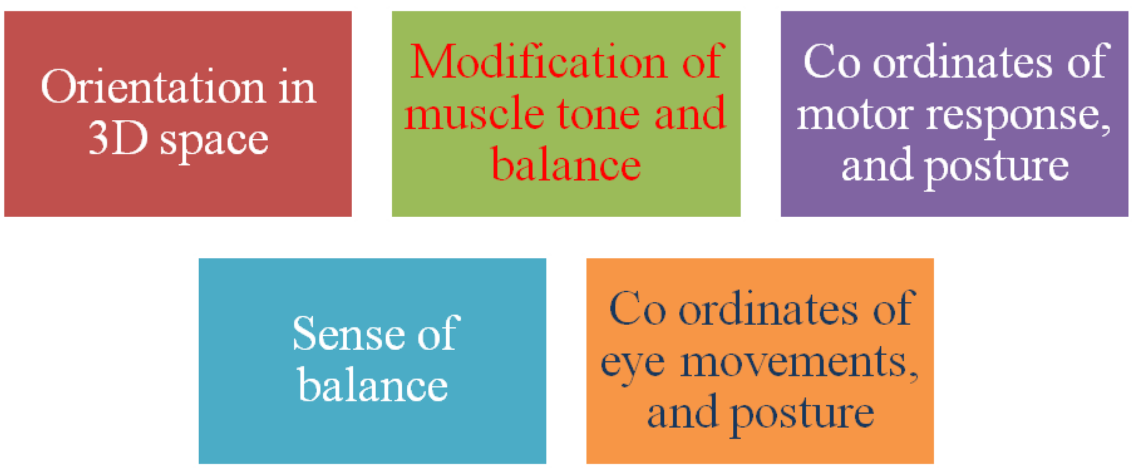

Fig. 1: Physiology of Vestibular system

Orientation cues were found compromised while floating in the weightlessness of space which neutralizesvestibular and somatosensory cues. While suspended at neutral buoyancy in the ocean somatosensory cueswere neutralized. The ability to sense orientation cues were found compromised in the elderly and clinical populations. Under such situations, enhancing the visual cues to orientation can be beneficial.[14]Sickness Induced by Centrifugation (SIC) susceptible subjects showed a marginally higher degree of utricular asymmetry, utricular sensitivity and semicircular canal sensitivity than the non-susceptible group. Thestudy results suggested that otolith asymmetry is one of vital factors and need not be present in all susceptible subjects in determination for susceptibility to SIC.[15]The study demonstrated that usage of special computerized stimulation programs with irritating visual and vestibular sensory inputs allowing to produce perceptive and sensorimotor responses can provide a promising tool for the evaluation of the state of the vestibular and related sensory systems.Thestability of static and dynamic spatial orientation in the presence of separate and combined visual and vestibular stimuli or without them also can be evaluated.[16]

ADAPTATION TO SPACE FLIGHT

Adaptation to cross-coupled stimuli was specific to the particular plane of head movement. The study findings had application to usage of centrifugation as a countermeasure for long duration spaceflights. Adapting astronauts to unconstrained head movements while rotating needed enough exposure to head movements in various planes and directions.[17]In a new method for measuring the time constant of head-movement-contingent oscillopsia (HMCO) produced by vestibular Coriolis stimulation, time constants could be fairly reduced by adding subject-stationary visual elements. This technique could be used to quantify adaptation to artificial gravity environmentsand applied to other types of oscillopsialike experienced by astronauts returning to Earth.[18]Role exerted by the pontine structures in determining adaptive changes following exposure to microgravity after launch as well as readaptation to the terrestrial environment after landing still needs to be investigated.[19]

Scientific studies done withastronauts after flight travel exposed that in some of them re-adaptation to the Earth gravitation involved increase of spontaneous oculomotor activity in immobile state of the head, suppression of otolithorganfunction in static 40 degrees bending of the head towards right or left shoulders. There was an enhancement of vestibular responsiveness with the rotation of head around the body longitudinal axis at the rate of 0.125 Hz.[20]Virtually each organ system functions differently in the absence of gravity, with some of these changes as maladaptive. Long duration spaceflight beyond low Earth orbit presents unique challenges from a biologic perspective. Astronauts traveling to Mars have to live in the absence of gravity for more than 12 months en route and will have to transition between weightlessness and planetary gravitational forces in the due course of the mission.the effects of spaceflight on nervous system function were discussed in the study done by Kalb R and Solomon D., 2007.[21]The sensory conflict hypothesis suggested that loss of tilt-related otolith signals upon entry into microgravity causes a conflict of actual and anticipated signals from sense organs serving the sense of spatial orientation. These sensory conflicts may induce motion sickness in other environments.[22]

MEDICAL LABORATORY DEVICES AND TESTS

Artificial touch information as a form of localised vibration on the torso that indicates down made the sense of orienting in microgravity faster, improved and easy. The importance of the artificial touch information increased over the initial one week of stay in microgravity. The weight of visual information decreased over the same duration.[23]Pseudorandom Galvanic vestibularstimulation(GVS) generatedmost of the salient features of post-flight locomotor dysfunction that were observed in astronauts following space missions. An ambulatory GVS system proved as a useful adjunct to the pre-flight astronaut training regimen.[24]An analysis of sensory input scores of somatosensory, visual, and vestibular functions demonstrated the specificity of GVS in distorting vestibular input to postural control. GVS induced an instability on computerized dynamic posturography(CDP) as profound bilateral vestibular loss, but was not so severe. The study suggested that unpredictably varying GVS quantitatively and qualitatively copies postural instability of vestibular origin.[25]Virtual reality techniques using immersive environments have potential for rehabilitation for patients with vestibulardisorders and aided in developing training regimens for astronauts to ameliorate side effects of exposure to microgravity. Driving skill was affected by use of benzodiazepines. In patients with vestibular impairments, driving was a problematic activity of daily living.[26]Devices using centrifugation or off-vertical axis rotation enhanced clinical neurological testing because it providedthe linear acceleration to stimulate specifically the otolith organs in a frequency range closer to natural head and body movement.[27]During the initial adaptation to the altered gravitational conditions in prolonged flight, the system of smooth visual tracking underwent a transition to a strategy of saccadic approximation, in which gaze tracked the movement of the target using a set of macro andmicrosaccadicmovements. The impairments in cosmonauts, resulted from vestibular deprivation with functional deafferentation of the otolith input in conditions of weightlessness.In cosmonauts conceptualizing space on the basis of perceiving the positions of the feet and head in addition showed support-tactile deprivation.[28]Meclizine alone had nill effect on task accuracy (Acc) or speed with or without spinning. Scopolamine alone reducedAcc, and with spinning, slowed speed. Promethazine alone had no adverse effect, but combined with spinning, reducedAcc and speed. Lorazepam alone reduced speed, and with spinning, also reduced Acc. The study suggested that, at clinically useful doses, the rank order of the drugs with the best cognitive profiles was meclizine>scopolamine>promethazine>lorazepam.[29]Rats maintained a normal allocentric frame of reference in zero gravity and normal gravity when on the floor. They lost sense of directional heading when placed on a wall or ceiling during acute exposures to zero gravity.[30]The number of investigators and physicians dealing with the functional problems of astronauts is minimal because of the limitations of working in the space environment. The number of investigators who are therapists and have experience with expertise in developing rehabilitation programs, is infinitesimal.This small group of investigators need to plan to make a coordinated, collaborative approach than investigators in larger fields.[31]Inputs from otolith organs and other graviceptorsare vital in regulating blood pressure during changes in posture in the Earth environment. Reflexes elicited by graviceptors, those affecting the cardiovascular system, are attenuated in spaceflight.[32]Neural processes occurring in spaceflight adaptation include deterioration in the ability of the nervous system to use rotational cues to estimate the relative orientation of gravity/tilt. Variations in the ability to estimate gravity also influence the ability of the nervous system to estimate linear acceleration.[33]Caloric tests done in Chinese fighter plane pilots indicated that there were function symmetry on both sides of semicircular canals, as well as normality of visual-vestibularandvestibulo-ocular reflexes in all the subjects. The parallel swing and Coriolis acceleration stimulus showed differences in vestibular functions among the pilots.[34]Exposure to microgravity significantly inhibited gene responses to light exposure seen after return to Earthgravity. A similar direct and indirect response pattern was found in central nucleus of the amygdala, related to the nucleus tractus solitaries (NTS). The rostral part of the NTS did not show direct gravityrelated changes in immediate-early gene (IEG) expression, instead showed an indirect effect of gravity on IEG responses to light. Similar pattern was seen in the intermediate reticular nucleus and the parvocellular reticular nucleus.[35]Among astronauts in the post-flight period ten symptoms were identified including clumsiness, difficulty concentrating, persisting sensation aftereffects, nausea, vomiting, vertigo while walking, vertigo while standing, difficulty walking a straight line, blurred vision, and dry heaves. The debriefing was in accordance to NASA Longitudinal Study of Astronaut Health database.[36]In the study done by Wang LJ et al. 2003., space vestibular experiments and works on perceptions of space motion sickness completed by Russian and American scientists were reviewed, in the hope to provide some references for future space medical researches.[37]Results of the study done on subjects pointing to targets during constant velocity rotation, showed that motor adaptation to high rotation rates was possible. Coriolis force perturbations of head movements occurred in a rotating environment but adaptation gradually developed over the course of many head movements.[38]As part of adaptation to altered gravitation conditions, a transition of the smooth visual tracing into the strategy of saccadic approximation, occurred. These disorders were due to avestibular deprivation.[39]Hlavacka F et al. 2001., tested how post-spaceflight postural reactions to galvanic stimulus in relation to vestibular input and to vibration of the lower leg muscles as a somatosensory input were changed.[40]Orthostatic intolerance in space medicine was caused by cardiovascular abnormal control. Vestibular adaptive changes under microgravity might have influenced the cardiovascular function and orthostatic intolerance.[41]

NYSTAGMUS AND OTOLITH ACTIVITY

Decrease in the severity of motion sickness and nystagmuswas noted during cosmonaut vestibular training (CVT). Even after one month of CVT, response to nystagmus were about 20-30% lower than control values. The study indicated that CVT induced a habituation of vestibular responses. This was a significant study on cosmonauts who were exposed to such vestibular training prior to their spaceflight.[42]Data compared in the normal fish and in acute chronically bilaterally blinded fish with those obtained in fish with intact and denervatedotoliths differentiatedwhether visual or neurovestibular system was dominant in response to altered gravity or drugs. Experiments contributed to validate the goldfish as a model for humans. Plasticity of the central nervous system allows astronauts to adapt to the altered visual stimulus conditions of zero gravity.[43]The decreased gravitational acceleration of orbit resulted in an upregulation of the sensitivity of utricular afferents. After a daypostflight, responses were similar to that in Earth gravity. The time course of return to normal afferent sensitivity was in parallel to reported decrease in vestibular disorientation in astronauts following return from space.[44]Exposure to space microgravity causedchanges in postural, locomotor and oculomotor functions. The vestibular abnormalities experienced by astronautsinvolved immediate reflex motor responses, including postural illusions, sensations of rotation, nystagmus, dizziness and vertigo, including space motion sickness. Adaptation to the microgravity environment occurred within one week.Upon return to Earth, re-adaptation took several months often.[45]

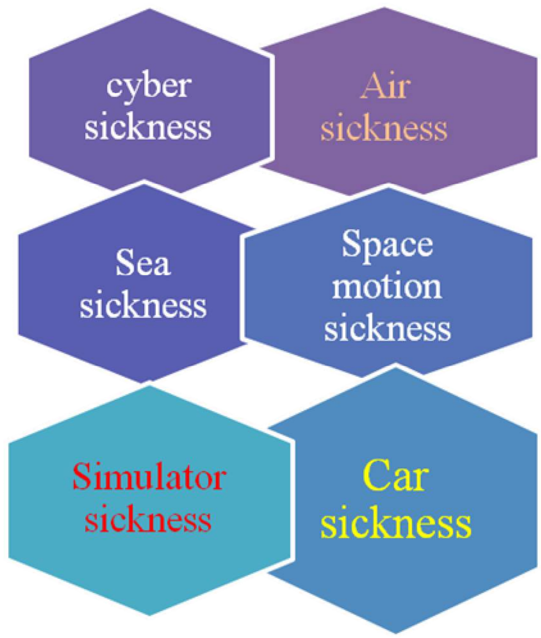

Fig. 2: Types of motion sickness

Adaptation to weightlessness involved reinterpretation of otolith activity, affecting tilt to be perceived as translation. Since linear acceleration during in-flight centrifugation was always perceived as tilt but not as translation, the findings in the study did not support hypothesis.[46]Thestudy done by Young LR., 2000., discussed major vestibular reactions that affect various human factors encountered in space missions starting from launch to early on-orbit, late on-orbit, EVA, artificial gravity, re-entry, and post-landing.[47]Dry immersion for duration of three days revealed that muscle sympathetic nerve activity (MSNA)to be enhanced after simulated microgravity while the response to orthostasis remained as unchanged. Bed rest and Neurolab Project clarified the similar pattern for longer duration of simulated microgravity. The alterations in MSNA were ascribed to the development of cardiovascular deconditioning after exposure to microgravity.[48]

CONCLUSION

The post flight investigations on crew from ISS, revealed functional disorders in the peripheral vestibular analyzer like an increased vestibular reactivity, absent or dampedotolith-cervical-ocular reflex, and in central vestibular analyser showing spontaneous typical and atypical nystagmus, gaze nystagmus.[49]Exposure to weightlessness in orbital flights had intense effects on the neurovestibular system and influenced head and eye movements, postural control, and spatial orientation. The associated space motion sickness was the signs of adaptation to this new environment. Reductions in post flight ocular counter rolling and changes in ocular counter rolling left/right asymmetries occurred after two weeks of space travel.[50]Higher brain functions of associative reactions, critical abilities, memory, as well as space orientation, body scheme control, geometric and arithmetic analysis and its reproduction, at last speech production, writing and reading were decreased in microgravity. Vegetative disorders, bone decalcification, primary muscular atrophy occurred along with alterations of sleep wake cycle with diminishing of vigility.[51]

REFERENCES

1. Weerts AP, Putcha L and Hoag SW. Intranasal scopolamine affects the semicircular canals centrally and peripherally. J Appl Physiol (1985). 2015;119(3):213-8. doi: 10.1152/japplphysiol.00149.2015. Epub 2015 May 7.
2. Carriot J, Jamali M and Cullen KE. Rapid adaptation of multisensory integration in vestibular pathways. Front Syst Neurosci. 2015;9:59. doi: 10.3389/fnsys.2015.00059. eCollection 2015.
3. Dilda V, Morris TR and Yungher DA. Central adaptation to repeated galvanic vestibular stimulation: implications for pre-flight astronaut training. PLoS One. 2014;9(11):e112131. doi: 10.1371/journal.pone.0112131. eCollection 2014.
4. Reschke MF, Cohen HS and Cerisano JM. Effects of sex and gender on adaptation to space: neurosensory systems. J Womens Health (Larchmt). 2014;23(11):959-62. doi: 10.1089/jwh.2014.4908.
5. Clément G and Wood SJ. Rocking or rolling--perception of ambiguous motion after returning from space. PLoS One. 2014;9(10):e111107. doi: 10.1371/journal.pone.0111107. eCollection 2014.
6. Lowrey CR, Perry SD and Strzalkowski ND. Selective skin sensitivity changes and sensory reweighting following short-duration space flight. J Appl Physiol (1985). 2014;116(6):683-92. doi: 10.1152/japplphysiol.01200.2013. Epub 2014 Jan 23.
7. Koppelmans V, Erdeniz B and De Dios. Study protocol to examine the effects of spaceflight and a spaceflight analog on neurocognitive performance: extent, longevity, and neural bases. BMC Neurol. 2013;13:205. doi: 10.1186/1471-2377-13-205.
8. De Saedeleer C, Vidal M and Lipshits M. Weightlessness alters up/down asymmetries in the perception of self-motion. Exp Brain Res. 2013;226(1):95-106. doi: 10.1007/s00221-013-3414-7. Epub 2013 Feb 9.
9. Kornilova LN, Naumov IA and Azarov KA. Gaze control and vestibular-cervical-ocular responses after prolonged exposure to microgravity. Aviat Space Environ Med. 2012;83(12):1123-34.
10. Cohen HS, Kimball KT and Mulavara AP. Posturography and locomotor tests of dynamic balance after long-duration spaceflight. J Vestib Res. 2012;22(4):191-6. doi: 10.3233/VES-2012-0456.
11. Mulavara AP, Ruttley T and Cohen. Vestibular-somatosensory convergence in head movement control during locomotion after long-duration space flight. J Vestib Res. 2012;22(2):153-66.
12. Clément G, Skinner A and Richard G. Geometric illusions in astronauts during long-duration spaceflight. Neuroreport. 2012;23(15):894-9. doi: 10.1097/WNR.0b013e3283594705.
13. Weerts AP, De Meyer G and Pauwels G. Pharmaceutical countermeasures have opposite effects on the utricles and semicircular canals in man. AudiolNeurootol. 2012;17(4):235-42. doi: 10.1159/000337273. Epub 2012 Apr 19.
14. Harris LR, Jenkin M, Dyde RT and Jenkin H. Enhancing visual cues to orientation: suggestions for space travelers and the elderly.Prog Brain Res. 2011;191:133-42. doi: 10.1016/B978-0-444-53752-2.00008-4.
15. Nooij SA, Vanspauwen R, Bos JE and Wuyts FL. A re-investigation of the role of utricular asymmetries in Space Motion Sickness. JVestib Res. 2011;21(3):141-51. doi: 10.3233/VES-2011-0400.
16. Kornilova LN, Naumov IA and Azarov KA. A computerized method for the combined evaluation of otoneurological and non-pharmacological correction of vestibulo-sensory and oculomotordisturbances.VestnOtorinolaringol. 2009;1:28-33.
17. Garrick-Bethell I, Jarchow T, Hecht H and Young LR. Vestibular adaptation to centrifugation does not transfer across planes of head rotation. JVestib Res. 2008;18(1):25-37.
18. Sanderson J, Oman CM and Harris LR. Measurement of oscillopsia induced by vestibular Coriolisstimulation. JVestib Res. 2007;17(5-6):289-99.

19. Centini C and Pompeiano O. Sleep research in space: expression of immediate early genes in forebrain structures of rats during the nasaneurolab mission (STS-90).Arch Ital Biol. 2007;145(2):117-50.
20. Kornilova LN, Temnikova VV and Sagalovich SV. Effect of otoliths upon function of the semicircular canals after long-term stay under conditions of microgravitation. RossFiziolZhIm I M Sechenova. 2007;93(2):128-40.
21. Kalb R and Solomon D. Space exploration, Mars, and the nervous system. Arch Neurol. 2007;64(4):485-90.
22. Heer M and Paloski WH. Space motion sickness: incidence, etiology, and countermeasures. AutonNeurosci. 2006;129(1-2):77-9. Epub 2006 Aug 28.
23. vanErp JB and van Veen HA. Touch down: the effect of artificial touch cues on orientation in microgravity. NeurosciLett. 2006;404(1-2):78-82. Epub 2006 Jun 27.
24. Moore ST, MacDougall HG and Peters BT. Modelinglocomotor dysfunction following spaceflight with Galvanic vestibular stimulation. Exp Brain Res. 2006;174(4):647-59. Epub 2006 Jun 9.
25. MacDougall HG, Moore ST, Curthoys IS and Black FO. Modeling postural instability with Galvanic vestibular stimulation. Exp Brain Res. 2006;172(2):208-20. Epub 2006 Jan 24.
26. Cohen HS. Disability and rehabilitation in the dizzy patient. CurrOpin Neurol. 2006;19(1):49-54.
27. Clément G, Reschke M and Wood S. Neurovestibular and sensorimotor studies in space and Earth benefits. Curr Pharm Biotechnol. 2005;6(4):267-83.
28. Kornilova LN. The role of gravitation-dependent systems in visual tracking. NeurosciBehav Physiol. 2004;34(8):773-81.
29. Paule MG, Chelonis JJ, Blake DJ and Dornhoffer JL. Effects of drug countermeasures for space motion sickness on working memory in humans. Neurotoxicol Teratol. 2004;26(6):825-37.
30. Taube JS, Stackman RW, Calton JL and Oman CM. Rat head direction cell responses in zero-gravity parabolic flight. J Neurophysiol. 2004;92(5):2887-997. Epub 2004 Jun 22.
31. Cohen HS. Update on the status of rehabilitative countermeasures to ameliorate the effects of long-duration exposure to microgravity on vestibular and sensorimotor function. J Vestib Res. 2003;13(4-6):405-9.
32. Yates BJ, Holmes MJ and Jian BJ. Plastic changes in processing of graviceptive signals during spaceflight potentially contribute to postflight orthostatic intolerance. J Vestib Res. 2003;13(4-6):395-404.
33. Merfeld DM. Rotation otolith tilt-translation reinterpretation (ROTTR) hypothesis: a new hypothesis to explain neurovestibular spaceflight adaptation. J Vestib Res. 2003;13(4-6):309-20.
34. Pei JC1, Chang L and Liu ZQ. Selection of vestibular system function in Chinese astronauts. Space Med MedEng (Beijing). 2003;16 Suppl:494-9.
35. Pompeiano O, d'Ascanio P and Balaban E. Gene expression in autonomic areas of the medulla and the central nucleus of the amygdala in rats during and after space flight. Neuroscience. 2004;124(1):53-69.
36. Bacal K, Billica R and Bishop S. Neurovestibular symptoms following space flight. J Vestib Res. 2003;13(2-3):93-102.
37. Wang LJ, Zhang D and Dong WJ. Study on space motion sickness before, during and after spaceflight. Space Med MedEng (Beijing). 2003;16(5):382-6.
38. DiZio P and Lackner JR. Sensorimotor aspects of high-speed artificial gravity: III. Sensorimotor adaptation. J Vestib Res. 2002-2003;12(5-6):291-9.
39. Kornilova LN. Role of gravitation-dependent systems in visual tracing. Ross FiziolZhIm I M Sechenova. 2003;89(3):280-91.
40. Hlavacka F, Dzurkova O and Kornilova LN. Vestibular and somatosensory interaction during recovery of balance instability after spaceflight. J Gravit Physiol. 2001;8(1):P89-92.
41. Wang LJ, Liu ZQ, He M and Ren W. Effects of adaptive changes of vestibular system on cardiovascular regulation and orthostatic tolerance. Space Med Med Eng (Beijing). 2001;14(3):225-9.

42. Clément G, Deguine O and Parant M. Effects of cosmonaut vestibular training on vestibular function prior to spaceflight. Eur J Appl Physiol. 2001;85(6):539-45.
43. Lathers CM, Mukai C, Smith CM and Schraeder PL. A new goldfish model to evaluate pharmacokinetic and pharmacodynamic effects of drugs used for motion sickness in different gravity loads. Acta Astronaut. 2001;49(3-10):419-40.
44. Boyle R, Mensinger AF and Yoshida K. Neural readaptation to Earth's gravity following return from space. J Neurophysiol. 2001;86(4):2118-22.
45. Holstein GR, Kukielka E and Martinelli GP. Anatomical observations of the rat cerebellar nodulus after 24 hr of spaceflight. J Gravit Physiol. 1999;6(1):P47-50.
46. Clément G, Moore ST, Raphan T and Cohen B. Perception of tilt (somatogravic illusion) in response to sustained linear acceleration during space flight. Exp Brain Res. 2001;138(4):410-8.
47. Young LR. Vestibular reactions to spaceflight: human factors issues. Aviat Space Environ Med. 2000;71(9 Suppl):A100-4.
48. Iwase S and Mano T. Microgravity and autonomic nervous system. Nihon Rinsho. 2000;58(8):1604-12.
49. Kornilova LN, Temnikova VV and Alekhina MI. Effect of long-term microgravity on the vestibular function. AviakosmEkolog Med. 2006;40(6):12-6.
50. Young LR and Sinha P. Spaceflight influences on ocular counterrolling and other neurovestibular reactions. Otolaryngol Head Neck Surg. 1998;118(3 Pt 2):S31-4.
51. Gerstenbrand F and Muigg A. Space medicine and life sciences in space.Wien Med Wochenschr. 1993;143(23-24):582-4.