Neurological Changes in Outer Space

Krishnan Ganapathy

M.Ch (Neurosurgery) FACS FICS FAMS PhD
Distinguished Visiting Professor IIT Kanpur INDIA

Abstract

Space travel is becoming a reality in our lifetime. When there is an acute shortage of neurologists worldwide (Ganapathy, 2015), discussing neurological changes in outer space could be considered outlandish. However, we need to be future ready. Understanding neurological changes due to microgravity and radiation exposure will eventually help improve understanding of neurobiology on earth. In an earlier publication (Ganapathy, 2018), the author demonstrated that Telemedicine has made distance meaningless. Closely monitoring health parameters in real-time and providing health care to astronauts and space tourists presupposes a basic knowledge of how various systems in the human body will behave in faraway space. Questions raised from constant exposure to zero gravity makes us think out-of-the-box. Fundamental issues are now being questioned including the influence of gravity on the central nervous system (Ganapathy, 2019). This communication essentially simplifies the complex technical global literature on this subject, making it easier for the interested reader.

Keywords: Neurology and microgravity, neurology and space travel, space medicine, neurological changes in space

Cambios neurológicos en el espacio exterior

Resumen

Los viajes espaciales se están convirtiendo en una realidad en nuestra vida. Ante la grave escasez de neurólogos a nivel mundial (Ganapathy, 2015), hablar de los cambios neurológicos en el espacio exterior podría parecer descabellado. Sin embargo, debemos estar preparados para el futuro. Comprender los cambios neurológicos debidos a la microgravedad y la exposición a la radiación contribuirá a mejorar la comprensión de la neurobiología en la Tierra. En una publicación anterior (Ganapathy, 2018), el autor demostró que la telemedicina ha hecho que la distancia carezca de sentido.

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Monitorear de cerca los parámetros de salud en tiempo real y brindar atención médica a astronautas y turistas espaciales presupone un conocimiento básico de cómo se comportan los diversos sistemas del cuerpo humano en el espacio lejano. Las preguntas que surgen de la exposición constante a la gravedad cero nos impulsan a pensar de forma innovadora. Actualmente se cuestionan cuestiones fundamentales, como la influencia de la gravedad en el sistema nervioso central (Ganapathy, 2019). Esta comunicación simplifica esencialmente la compleja literatura técnica global sobre este tema, facilitándole la comprensión al lector interesado.

Palabras clave: Neurología y microgravedad, neurología y viajes espaciales, medicina espacial, cambios neurológicos en el espacio.

外太空中的神经系统变化

摘要

太空旅行正在成为我们有生之年中的现实。当全球神经病学家严重短缺时(Ganapathy,　2015)，讨论外太空中的神经系统变化可能会被认为是荒唐的。然而，我们需要为未来作好准备。了解由微重力和辐射暴露导致的神经系统变化最终将有助于提高对地球神经生物学的理解。在作者之前发表的一篇出版物(Ganapathy,　2018)中，其证明了远程医疗使距离变得毫无意义。密切实时监测健康参数并为宇航员和太空游客提供医疗保健的前提是了解人体中的各个系统在遥远空间中的行为方式。持续暴露在零重力下引发的问题让我们跳出固有的思维模式。一些基本问题正受到质疑，包括重力对中枢神经系统的影响(Ganapathy,　2019)。本文从本质上简化了有关这一主题的复杂技术文献，使感兴趣的读者更容易理解（内容）。

关键词：神经病学与微重力，神经病学与太空旅行，太空医学，太空中的神经系统变化

Objective

The primary objective of this communication is to give an overview and summarise the current knowledge in the area of extra-terrestrial neurosciences for a non-specialist. An earlier publication on this subject had primarily catered to medical and surgical neurologists (Ganapathy et al., 2019).

Methods

This is not a formal meta-analysis of all published papers, using specific key words from various data bases. This is a review of a number of articles and case reports of various neurological clinical conditions, identified in astronauts, who spent considerable time outside the confines of the earth. Experimental laboratory investigations, in a space simulated environment, have also been studied. The author, a neurosurgeon with almost five decades of clinical experience, after a few interactions with NASA Flight surgeons and astronauts, has shortlisted areas, clinically relevant. This submission is neither qualitative, quantitative, comparative, mixed, collaborative, action-oriented, critical in substance nor a research submission.

Introduction

Humans are the most adaptable species on earth, able to live in vastly different environments. Space is the ultimate frontier challenging human adaptive capabilities. However, human cognitive and perceptual motor performances are not designed for the hostile environment in space (McGregor et al., 2023). In the last 65 years, space exploration has advanced human knowledge. From 1961 to August 2024, a total of 685 individuals from 41 countries have spent 48,947 person days in space over 1,290 spaceflights. Nineteen medical emergencies (nonfatal) have been documented in these "super healthy" astronauts. Russian cosmonaut Oleg Kononenko has spent more than 1,000 days in the International Space Station on 5 missions in space. Several private organisations have announced plans to commence space tourism. Space tourists are less likely to be "super healthy." NASA's reference mission to Mars is expected to last 1,100 days. Adverse cognitive, behavioural, and mental health problems need to be considered. Social isolation, immobilization, and altered gravity can have profound effects on brain plasticity, associated with spatial navigation (Stahn & Kühn 2021). Understanding cerebral changes that occur when travelling beyond Earth's gravity would make space travel safer.

Extra-terrestrial Radiation and the Brain

Vazquez (1998) pointed out that future space missions would involve long-term travel beyond the earth's magnetic field. Radiation hazards include solar flares, galactic cosmic rays, altered gravitation fields, and physiological stress. Biological effects of extended exposure to high-energy heavy ions on the nervous system are not clear, though laboratory studies suggest an oncogenic potential of galactic cosmic rays.

Extra-terrestrial Neuropharmacology

Pharmacokinetics and pharmacodynamics of usage of drugs acting on the nervous system in space have yet to be studied. Medications are administered on the assumption they act, as on Earth. Decreased drug and formulation stability in space could influence the efficacy and safety of medications (Kast et al., 2017).

Extra-terrestrial Neurophysiological changes

Weightlessness, electromagnetic fields and radiation found in Space could influence structure and function of the Central Nervous System (CNS). Physiological changes occur during and after long-term spaceflight, including neuro vestibular disturbances, cephalic fluid shifts, cardiopulmonary pressure modifications, alterations in sensory perception and proprioception, psychological disturbances and cognitive changes. Animal studies show altered plasticity of the neural cyto architecture, decreased neuronal metabolism in the hypothalamus, and changes in neurotransmitter concentrations.

The acute and chronic effects of hypobaric exposure upon the brain in a microgravity setting has been evaluated (Sherman & Sladky, 2018). These include Decompression Sickness, which may progress to severe neurological or pulmonary symptomatology. The brain (confusion, memory loss, visual changes, diplopia, scotomas, headache, seizures, vertigo, unconsciousness), spinal cord (dysesthesias, paresthesias, constriction and pain around the chest or abdomen, ascending paralysis, bowel and bladder incontinence) and peripheral nerves (fasciculations and paresthesias) can all be affected by hypobaric exposure during space travel. Cortical reorganization in an astronaut's brain after long-duration spaceflight has been documented (Demertzi, 2016). Differences were found in functional connectivity between the motor cortex and cerebellum in the resting state. Changes in the supplementary motor areas were observed during a motor imagery task. These results highlight the underlying neural basis, for the observed physiological deconditioning due to spaceflight. Preliminary spaceflight studies have shown involvement of cerebellum, cortical sensorimotor, somatosensory areas and vestibular pathways.

Extra-terrestrial Effects of Gravity on the Nervous System

Short-term effects of microgravity on neural control have been studied during Low Earth Orbit missions. Consequences of prolonged microgravity and space radiation needs to be studied at the molecular, cellular and tissue levels. Microgravity in space affects every single organ and body system in different intensities and manner, during short- and long-term missions. Kohn (2018) has stressed the importance of understanding impact of reduced gravity on the nervous system. This is essential for ensuring human survival in hypogravity environments of Mars and the Moon. Persistent modulation in the sensory and motor systems and resulting structural loss of muscle and bone mass have been reported. In addition, there is recalibration of sensory perception, vestibular and proprioceptive functions, changes in muscle synergies and coordination, decline of muscle force, changes in posture control, locomotion and functional mobility. These adaptations are of clinical relevance. Russomano et. al. (2015) have pointed out that the application of lower body negative pressure partially reverses the headward shift of blood and body fluids occurring in microgravity. This reduces cardiovascular deconditioning and has been applied as a countermeasure during spaceflights. Fujii et al. (1992) emphasize that effective treatments depend on understanding mechanisms by which microgravity adversely affects the nervous system. Ataxia, postural disturbances, perceptual illusions, neuromuscular weakness, fatigue, and ocular changes have been attributed to the effects of microgravity. They play an important role in astronaut health and re-adaptation to the terrestrial environment. Murthy et al. (1992) have discussed increased intracranial pressure in humans during simulated microgravity.

Extra -terrestrial Intracranial Hypertension

Spaceflight-induced intracranial hypertension is a distinct clinical phenomenon. Spaceflight-induced visual pathology is a manifestation of increased intracranial pressure (ICP) (as on earth). Mechanisms postulated include an upward shift of body fluids, venous outflow obstruction, blood-brain barrier breakdown and disruption to CSF flow. NASA coined the phrase "**V**isual **I**mpairment and **I**ntracranial **P**ressure [**VIIP**] syndrome" to describe optic-disk edema and elevated intracranial pressure in astronauts returning from the International Space Station (Zhang & Hargens, 2018)**.** This clinical entity has now been renamed as **Spaceflight Associated Neuro-ocular Syndrome (SANS**). Understanding SANS has become a high priority for NASA in view of future long-duration missions. Wostyn and Devyn (2017) emphasise that the Optic Nerve Sheath response to the rise in ICP during extended microgravity exposure may help determine, whether or not an astronaut is susceptible to developing ophthalmic changes of SANS. A strong relationship between body weight and the subsequent development of ocular changes in space has been reported (Buckey et al., 2018).

Lawley et al. (2017) have reiterated that raised ICP is the most mission critical medical problem identified in manned spaceflight. Astronauts often develop impaired vision, resembling syndromes of elevated ICP on Earth. Gravity has a profound effect on fluid distribution and pressure within the human circulation. ICP over 24 hours in microgravity is slightly above that observed on Earth, accounting for the remodelling of the eye in astronauts. It is postulated that the human brain is protected by daily circadian cycles. Studies have reviewed a spectrum of ocular and cerebral responses to extended microgravity exposure. *300 post-flight questionnaires documented that approximately 29% and 60% of astronauts on short-duration and long-duration missions, experienced a degradation in dis-*

*tant and near visual acuity (*Lee et al., 2016, 2017). Kramer et al. (2015, 2012) have documented MR derived cerebrospinal fluid hydrodynamics as a marker and a risk factor for intracranial hypertension in astronauts exposed to microgravity. This infers a downregulation in CSF production in a microgravity environment, which is upregulated upon return to normal gravity.

Space Headache: A New Secondary Headache

Headaches are a common complaint during spaceflights (Vein, 2009), usually attributed to space motion sickness (SMS) In one study of 17 astronauts, 12 (71%) had experienced at least one headache episode, only in space. Most headache episodes (76%) were not associated with symptoms of SMS, migraine or tension headache. Spaceflight appears to trigger headaches in otherwise "super healthy" males. This has led to the identification of a distinct clinical entity "Space Headache." Wilson et al. (2011) propose that headache of high altitude and microgravity is similar to clinical syndromes of cerebral venous hypertension.

Extra -terrestrial Effects on the Neurovestibular System

During spaceflight the gravitational force (normally acting on earth) stops acting, resulting in a variety of clinical symptoms. This includes space motion sickness, postural illusions, sensations of rotation, nystagmus, dizziness, vertigo, salivation, epigastric discomfort, vomiting, apathy, lethargy, sleepiness, fatigue, weakness, headache (especially frontal) and reduction in muscular coordination and performance (Graybiel, 1979). NASA has identified a potential risk of spatial disorientation, motion sickness, and reduced performance in astronauts during re-entry and landing of the proposed Orion crew vehicle. Angular accelerations of the crew vehicle during re-entry were simulated. The group that was given Autogenic-Feedback Training Exercises (AFTE) had significantly reduced clinical problems (Cowings, 2018).

Imaging studies of brain following space travel

MRI brain imaging of astronauts on return to earth indicate structural neuroplasticity. Compensatory neurogenesis counter weighs expected normative volume loss with age. White Matter Hyperintensities have also been linked to cortical and subcortical functions, particularly executive function, processing speed, and overall cognition along with motor/gait function (Sherman & McGuire, 2015). Changes in volume of the central sulcus and CSF spaces at the vertex, and vertical displacement of the brain have been documented. Cine clips showed an upward shift of the brain after long-duration flights besides optic-disk oedema. Mission duration is a key factor in space flight-associated imaging changes in brain MRI. Structural and functional changes occur both in the primary regions and in integration of those regions during higher-level functions. They could represent beneficial adaptations or maladaptive dysregulations to the novel environment (Roy-O'Reilly, 2021). Ventricle expansion is proportional to duration of spaceflight but appears to taper off after 6 months in space. Inter-mission intervals less than 3 years may not allow sufficient time for ventricles to fully recover their compensatory capacity (De la Torre, 2014). Brain morphology, cerebral metabolism, and *in vivo* neurochemistry in the human brain can now be studied with Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), and next-generation Magnetic Resonance Imaging (MRI). This helps investigate alterations occurring in the CNS due to spaceflight (Newberg & Alavi, 1998)

Extra-terrestrial Back Pain

Astronauts have a 53-68% increased risk of experiencing moderate to severe Low Back Pain and a fourfold increased risk of developing herniated intervertebral discs during microgravity exposure and within one year post-flight (Johnston, 2010). On the ISS, astronauts do 150 minutes of exercise each day including running, cycling and strength training. This is to reduce bone loss and loss of muscle mass. In spaceflight the spine lengthens, normal posture is lost and intervertebral discs change their morphology. As human spine anatomy has adapted to an upright posture on Earth, observations of how spaceflight affects the spine, could provide new and potentially important information on spine biomechanics. This could benefit earthlings! In one study, of NASA astronauts supine lumbar lordosis decreased (flattened) by 11%.

Conclusion

Studying extra-terrestrial neurosciences may be viewed sceptically. There is already evidence that knowledge of neurological changes due to microgravity and radiation are leading to additional insights into how the nervous system functions on Earth. We need to be future ready as the future is always ahead of schedule.

References

Buckey, J.C., Phillips, S.D., Anderson, A.P., Chepko, A.B., Archambault-Leger, V., Gui, J., et al. (2018). Microgravity-induced ocular changes are related to body weight. *Am J Physiol Regul Integr Comp Physiol.* 315: 2018. DOI: 10.1152/ajp regu.00086. https://www.physiology.org/doi/full/10.1152/ajpregu.00086.2018.

Cowings, P.S., Toscano, W.B., Reschke, M.F., & Tsehay, A. (2018). Psychophysiological assessment and correction of spatial disorientation during simulated Orion spacecraft re-entry. *Int J Psychophysiol, 131*, 102-112.

De la Torre, G.G. (2014). Cognitive neuroscience in space. *Life , 4*, 281-294. https://doi.org/10.3390/life4030281.

Demertzi, A., Van Ombergen, A., Tomilovskaya, E., Jeurissen, B., Pechenkova, E., Di Perri, C., et al. (2016). Cortical reorganization in an astronaut's brain after long-duration spaceflight. *Brain Struct Funct, 221*: 2873-6.

Fujii, M.D. & Patten, B.M. (1992). Neurology of microgravity and space travel. *Neurol Clin,10*, 999-1013.

Ganapathy, K. (2015). Distribution of neurologists and neurosurgeons in India and its relevance to the adoption of telemedicine. *Neurol India*, *63*, 142-54.

Ganapathy, K. (2018). Telemedicine and neurosciences. *Neurology India, 66*, 642-51.

Ganapathy, K. (2019). Editorial extra-terrestrial neurosciences. *Neurology India*, 67 (Suppl 2), S165-S166, DOI: 10.4103/0028-3886.259118.

Ganapathy, K., da Rosa, M., and Russomano, T. (2019). Neurological changes in outer space. *Neurol India,. 67*(1), 37-43. DOI: 10.4103/0028-3886.253647. PMID: 30860089.

Graybiel, A. (1979). Motion sickness susceptibility during rotation at 30 rpm in free-fall parabolic flight. *Acta Astronaut, 6*, 1481-1487.

Johnston, S., Campbell, M., Scheuring, R., and Feiveson, A. (2010). Risk of herniated nucleus pulposus among US astronauts. *Aviation, Space and Environments Medicine*, *81*, 566-574.

Kast, J., Yu, Y., Seubert, C.N., Wotring, V.E., and Derendorf, H. (2017). Drugs in space: Pharmacokinetics and pharmacodynamics in astronauts. *Eur J Pharm Sci., 109*, 2-8.

Kohn, P. M. F., Koch, C., and Ritzmann, R. (2018). The effect of gravity on the nervous system. *Intech Open, 6*, 87-101.

Kramer, L.A., Hasan, K.M., Sargsyan, A.E., Wolinsky, J.S., Hamilton, D.R., Riascos, R.F., et al. (2015). MR-derived cerebral spinal fluid hydrodynamics as a marker and a risk factor for intracranial hypertension in astronauts exposed to microgravity. *J Magn Reson Imaging, 42*, 1560-71.

Kramer, L.A., Sargsyan, A.E., Hasan, K.M., Polk, J.D., and Hamilton, D.R. (2012).

Orbital and intracranial effects of microgravity: Findings at 3-T MR imaging. *Radiology, 263*, 819-827.

Lawley, J.S., Petersen, L.G., Howden, E.J., Sarma, S., Cornwell, W.K., Zhang, R., et al. (2017). Effect of gravity and microgravity on intracranial pressure. *J Physiol, 595*, 2115-2127.

Lee, A.G., Tarver, W.J., Mader, T.H., Gibson, C.R., Hart, S.F., and Otto, C.A. (2016). Neuro-Ophthalmology of Space Flight. *J Neuroophthalmol, 36*, 85-91.

Lee, A.G., Mader, T.H., Gibson, C.R., and Tarver, W. (2017). Space flight-associated neuro-ocular syndrome. *JAMA Ophthalmology, 135*, 992-994.

McGregor, H.R., Hupfeld, K.E., and Pasternak, O. et al. (2023). Impacts of spaceflight experience on human brain structure. *Sci Rep, 13*, 7878. https://doi.org/10.1038/s41598-023-33331-8.

Murthy, G., Marchbanks, R.J., Watenpaugh, D.E., Meyer, J.U., Eliashberg, N., and Hargens, A.R. (1992). Increased intracranial pressure in humans during simulated microgravity. *The Physiologist, 35*, 184-185.

Newberg, A.B. and Alavi, A. (1998). Changes in the central nervous system during long-duration space flight: implications for neuro-imaging. *Adv Space Res, 22*, 185-96.

Roy-O'Reilly, M., Mulavara, A., and Williams, T. (2021). A review of alterations to the brain during spaceflight and the potential relevance to crew in long-duration space exploration. npj *Microgravity, 7*, https://doi.org/10.1038/s41526-021-00133-z.

Russomano, T., May, F., Dalmarco, G., Baptista, R. R., Gauger, P., Petrat, G., and Beck L. A (2015). Gender comparison of Cardiovascular Responses to Lower Body Negative Pressure Exposure. *American Journal of Medical and Biological Research, 3*, 95-101.

Sherman, P. and Sladky, J. (2018). Acute and Chronic Effects of Hypobaric Exposure upon the Brain. *IntechOpen, 4*, 45-70.

Sherman, P.M. and McGuire, S. (2015). Subcortical white matter hyperintensity burden in astronauts. *Aerospace Medicine and Human Performance, 86*, 309.

Stahn, A.C., and Kühn, S. (2021). Brains in space: The importance of understanding the impact of long-duration spaceflight on spatial cognition and its neural circuitry. *Cognitive Processing, 22* (Suppl 1), S105–S114 https://doi.org/10.1007/s10339-021-01050-5.

Vazquez, M.E. (1998). Neurobiological problems in long-term deep space flights. *Adv Space Res., 22*, 171-83.

Vein, A.A., Koppen, H., Haan, J., Terwindt, G.M., and Ferrari, M.D. (2009). Space headache: A new secondary headache. *Cephalalgia, 29*:683-6.

Wilson, M.H., Imray, C.H., and Hargens, A.R. (2011). The headache of high altitude and microgravity: Similarities with clinical syndromes of cerebral venous hypertension. *High Altitude Medicine & Biology, 12*, 379-386.

Wostyn, P. and De Deyn, P. P. (2017). Optic Nerve Sheath Distention as a Protective Mechanism against the Visual Impairment and Intracranial Pressure Syndrome in Astronauts. *Invest Ophthalmol Vis Sci, 58*, 4601-4602.

Zhang, L.F. and Hargens, A.R. (2018). Spaceflight-Induced Intracranial Hypertension and Visual Impairment: Pathophysiology and Countermeasures. *Physiol Rev., 98*, 59-87.

Conflicts of Interest

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Ethical Obligations

The sole author is the corresponding author and is responsible for the content of the submission and all revisions.

Correspondence to K. Ganapathy, Distinguished Visiting Professor, IIT, Kanpur. E-mail drkganapathy@ gmail.com; ganapathy@iitk.ac.in