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Neuroscience & outer space travel: The final frontier

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ABSTRACT

Space travel is soon going to be a reality. With already 700 people signed up for commercial trip the scientific community is being pushed to limits which knows no boundaries. Over the past Six Decades outer space has slowly been unraveling itself in a manner which has transformed from a generating a response of fear to that of challenge. Because of the harsh environment in space, astronauts are at risk of both short-and long-term health risks. The 2 major challenges associated with spaceflight are radiation effects and the physiologic consequences of a microgravity environment. Many of the immediate risks (decompression, thermal injury, arcing injuries) are mitigated by the design of the spacecraft and spacesuits. The biologic effects of long-term exposure to space radiation are still unclear. It may range from, development of cataracts and concerto altered neurobiology.

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1. Introduction

The dream to travel to outer space will become a achievable reality for general population. With already 700 people signed up for commercial trip the expert community is being pushed to greater horizons extending the known boundaries. Over the past Six decades outer space has slowly been unraveling itself in a manner which has transformed from generating a response of fear to that of challenge. Due to severity and nature of space environment astronauts and space travelers are at risk of both short- and long-term health risks. The difficulties associated with spaceflight are because of radiation and the physiological changes caused by micro gravity. Many of the effects of short term and imminent risks (decompression, thermal injury, arcing injuries) are somewhat reduced by the specific design of the spacecraft and spacesuits. The biological effects of long-term exposure because of two space radiation are still

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being evaluated and studied. It ranges from, development of cataracts and cancer to altered neurobiology.

From the beginning of era of space travel from 1961 to June 2018, 561 individuals from more than 40 countries have been to outer space. There has been over 1230 spaceflights leading to total of 46,947 person-days in space. As per literature available during spaceflights, a total of 17 nonfatal yet severe medical emergencies have been documented. 1 Several private organizations have announced plans to commence space tourism.² Space tourism is soon to become a reality. In the future, all humans travelling to space may not be super healthy as the astronaut. Hence ensuring medical fitness during the course of space travel is going to be a big challenge. Outer Space environment throws unexpected challenges to human body especially the central nervous system. These include weightlessness, electromagnetic fields and radiation hazards. Although effect of short term exposure, have been studied, the long term consequence on the neuraxis & neural pathways is yet to be understood. In order to ensure

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uneventful and healthy outer space travel, we must have an understanding of the altered neurophysiology in outer space, know its impact on the nervous system and further device interventions to avoid and treat the deleterious effects arising from the same.

By December 2023 India aims to take a giant leap by ushering its Vyomanauts into the outer space, the final frontier, and making history. In near future we will see & probably experience more of space travel and tourism. In order to be future ready the preparation has to start right now. Space is an unforgiving harsh and challenging environment that leaves very limited margin for human error or technical failure.

The space environment with features such as microgravity leading weightlessness, strong electromagnetic fields, and radiation that affects the structure and functionality of the central nervous system (CNS) at a very cellular level. Physiological changes at a cellular level are known to occur after spending variable time in space, which includes vestibular disturbances, brain and spinal fluid shifts, cardiopulmonary pressure changes, modifications in sensory perception and proprioception, and cognitive and psychological disturbances. Animal studies have shown altered plasticity of the neural cellular architecture, causes changes in firing speed of neuron, reduced neuronal metabolism in the hypothalamus, and changes in neurotransmitter functions. Recent progress and studies which includes positron emission tomography show there is a change in brain morphology, cerebral metabolism, and neurochemistry in vivo in the human brain. Single photon emission computed tomography, and next-generation magnetic resonance imaging (MRI) could provide the opportunity of studying the alterations that occur in the central nervous system (CNS) due to spaceflights.³

2. Materials and Methods

Since 1961 till date more than 560 people from 40 countries have travelled to outer space. Experiences gained by them coupled with animal studies have revealed some of the alterations taking place in the neural network and physiology. Findings of these studies gathered through literature search are collated in this research paper. Attempt has been made to explain the possible adaptive mechanisms in Central Nervous System. Based on current evidence, countermeasures to mitigate the effects of microgravity and radiation have been proposed. This may need further studies for validation.

3. Observation

Most of the Data collected have been from the finding published by International Space agencies over the past Six Decades. Attempts are being made to simulate microgravity on land. For the purpose of experimentation four ground based alternatives exist as on date as given below.

3.1. Ground-based space alternatives for human studies

Dry immersion generally involves immersing the subject in thermo-neutral water while being insulated in an waterproof fabric in order to decreasr or minimize and overcome the unwanted consequences of long-term direct water exposure. 4

Head Down Bed Rest. (HDBR) consists of a subject being in a bed that is inclined at a certain angle (-6° in most cases). This can be done for short-term investigations (e.g. 72 hours)⁵ or long-term studies (e.g. 90 days).⁶ The head down tilt induces an upward fluid shift, which mimics the changes seen in space travel. This change in cephalic fluid shift in individuals going on space flight causes a plethora of symptoms ranging from increased intracranial pressure, various degrees of visual impairment (together named the VIIP syndrome), alterations in cerebral oxygenation and changes in CBF.

Parabolic Flight. During a Parabolic Flight (PF), due to a specific flight trajectory the acceleration of the aircraft negates the acceleration caused due to gravity. This results in, normo-, hyper- and microgravity phases experienced by the subjects on board of the PF aircraft. The hyper gravity phase precedes and follows the microgravity phase, characterized by 1.5 to 1.8 g and lasts around 30–35 s. ¹

Another approach to mimic spaceflight-related features is to study human deployment in conditions such as Antarctic overwintering, undersea missions, Sensory deprivation, confinement for prolonged periods, and altered circadian cycles. These conditions are all replicated to high precision and as a result these missions results in an almost acceptable spaceflight analog (except for space-related changes in gravity). ¹

3.2. Microgravity and Neuroplasticity

In 1998, a 16-day space mission called Neurolab (STS-90) was launched to study the physiological and psychological changes of microgravity on the nervous system. Tests were conducted before, during, and after spaceflight to precisely find out how microgravity affects the various aspects of neural functioning. Neurolab investigated and studied sensory integration and navigation, blood pressure dynamics, the neurovestibular system, circadian rhythms and sleep, and nervous system development in weightlessness. The experiments specifically and in great detail proved that astronauts return to Earth with a nervous system greatly different than the one they left with.

CSF production decreases to a variable extent in the microgravity environment of space but increases and reaches a almost near normal level when astronauts return to normal gravitational conditions.⁷

"Floating Brain Phenomenon". Microgravity causes a shift in fluid from the lower body to the upper body. ⁸ Wiith decrease in CSF space there is an upward vertical shift of the brain. This is called the floating brain phenomenon. Due to this upward shift of brain veins or venules may get compressed, resulting in obstruction of CSF and venous outflow. This results in an increase in, intracranial pressure which can cause swelling of the optic nerve resulting in various ocular symptoms. ⁹

Studies conducted so far have shown alterations in brains structure and function which have been validated by existing investigative modalities. The understanding is far from understood.

3.3. Inferences drawn on basis of current findings

Functional MRI has shown that there is a reduced cortical activity in the motor areas associated with leg representation and a decrease in corticospinal excitability after HDBR. Larger the increase in motor cortex excitability, the smaller the functional mobility impairment. To reduce the effects of this change of lower extremity dysfunction Trans Magnetic Stimulation (TMS) could be used as a possible countermeasure.

Decrease in thalamic connectivity during resting-state can be due to reduced motor control abilities and decrements in executive function in astronauts.

The Ventromedial Pre Frontal Cortex (VMPFC) is the principal component of the decision-making circuitry during precise decision-making. The finding of less deactivation of the VMPFC after HDBR can be due to the neural adaptation process and changes in neuroplasticity after spaceflight. Furthermore, risk-taking and precise decision making is due to a higher level of cognitive functioning and has an important role in extreme challenging and demanding environments such as spaceflight. These findings suggests a detrimental effects of simulated spaceflight on complex and risky decision-making.³

Changes also occur in the anterior insular and middle cingulate cortex (MCC) network and both key regions of the resting state network. This can be because of the apparent cephalic fluid shift which in turn results in increase in CBF and intracranial pressure. Autonomic nervous function (i.e. sympathetic and parasympathetic) decreases in intrinsic functional connectivity in the ANS and the MCC network.³

A decrease and increase in the posterior cingulate cortex and anterior cingulate cortex, respectively could result in changes in the autonomic nervous system, seen in space travelers. In addition there is also an increase in activity in the left cerebellar posterior lobule, indicating a role by the cerebellar posterior lobule to compensate the reduction in functional connectivity in the para central lobule. This compensatory role of the cerebellum is apparently necessary for fine motor control and this could be one of the reasons

for significant impairment of fine motor in astrounouts in micro gravity. ¹⁰

MRI studies after and before flight have shown that brain undergoes an upward shift and posterior rotation relative to skull resulting in narrowing of CSF spaces at the vertex, which results in stretching of the pituitary stalk, and rotation of the cerebral aqueduct after flight.

There was a decrease in brain connectivity between the temporoparietal regions, part of the vestibular network, and an increase in functional connectivity between the right parietal operculum, a key region of the vestibular cortex, and the ipsilateral cerebellum. These findings, along with the results described above suggest that spaceflight-related sensorimotor problems after and during a space flight can be due to cortical changes at the central level. ¹¹

HDBR studies has primarily shown that changes related to motor-related tasks which includes fine motor control, complex cognitive function such as executive functions spatial working memory and multi tasking, can be because of changes in sensorimotor, somatosensory and cognitive-related brain regions in cortical areas such as the insula.

However, specific conclusions in regards to spaceflight need to be made by carefully analyzing results obtained from space simulating environment and to actual spaceflight and also because of limited sample size in some of the current studies.

Changes in WM structure can take place after 90 min of a spatial learning task. ^{12,13}

3.4. Countermeasures proposed

Motor Imagery (MI). MI is a process in which a specific and pre-decided action is internally reproduced in working memory, from a first-person perspective, without subjecting the individual to any overt motor output. ¹⁴

Trans Magnetic Stimulation -TMS can be used as a protective measures for astronauts on long-duration space missions to improve the lower extremity dysfunction which occurs during space flight. ¹⁵

Artificial Gravity- Exposing astronauts to continuous or brief periods of artificial gravity might reverse or halt any neuronal changes in space travelers. ¹⁶ For example, this could be done by introducing a centrifuge on board. ¹⁷

To counter the assaults and changes on the cardiovascular and musculoskeletal systems, astronauts must exercise for at least 2.5 hours a day, 6 days a week.

Astronauts aboard the ISS and scientists stationed on Earth will study a bone-forming molecule called NELL-1 and analyze its practical use to promote bone formation and its role against possible bone degeneration.

Water or plastics in the future and plasma shield, confined by a magnetic field, can be used to negate the effects of incoming radiations of incoming particles.

Other tested countermeasures includes lower body negative pressure treadmill running, exercises with artificial resistance with external vibration, resistance exercise alone, rowing like exercises using a flywheel device and self-performed exercises which are designed to mobilize the spine.

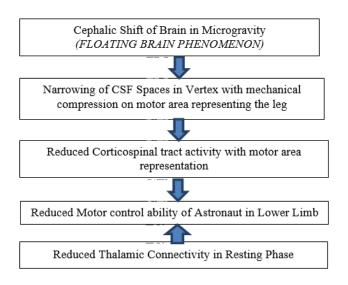


Diagram 1: Schematic Diagram showing the probable mechanism leading to reduced ability to move lower limbs among astronauts in long period outer space missions.

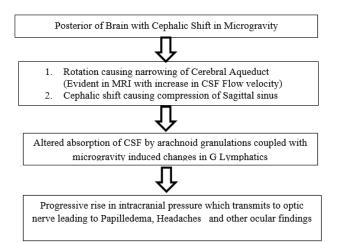


Diagram 2: Schematic Diagram showing the probable mechanism leading to raised Intra Cranial Pressure and Papilledema among astronauts in long period outer space missions.

4. Discussion

4.1. Spine in outer space

There are significant changes in musculoskeletal system of astronauts spending variable time in space. These changes are more or less concentrated in lumbar and pelvic regions

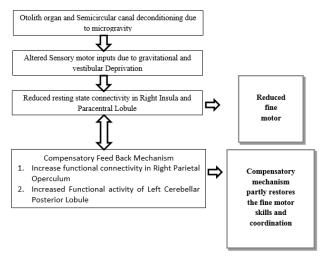


Diagram 3: Showing the structural and functional adaptation of the Central Nervous System (Neuroplasticity) to prolonged period of microgravity.

because of microgravity. Most of the astronauts experience low back pain, because of increase in the incidence of intervertebral disc injury while coming back to earth.

As the spine lengthens, normal posture and curvature is lost, there is a change in intervertebral discs morphology. Also Lumbar Multifidus (LM) and Transversus Abdominis (Tr A) muscles atrophies leading to flexor-extensor lumbopelvic muscle imbalances during spaceflight.

Current in-flight countermeasures are designed to prevent physiological changes to microgravity. But they are not designed for changes taking place in lumbopelvic adaptations during space flight. Following which astronauts, have to undergo prolonged periods of rehabilitation once they return to Earth's gravity to reduce injury risk. ¹⁸

4.2. EEG & neurophysiology

With increased gravity there is initial increase in EEG activities more so in higher frequencies. However at around 4g there is loss of consciousness leading to slowing of EEG due to hypoxia. In microgravity, the common changes in EEG are faster frequencies such as alpha and beta waves. The results from simulated microgravity (bed rest) point to specific changes in theta and alpha waves signaling cortical inhibition. The changes in EEG activity in space flight are a result of reduced sensorimotor input. Because of limited research about gravity-related EEG changes it is difficult to draw any unequivocal conclusions. Furthur systematic review studies about electro cortical activity in space and parabolic flights, along with longer bed rest studies are needed in order to increase knowledge about brain functioning in extreme conditions such as space flights. 19

4.3. Vestibular physiology

There was a reduced functional connectivity in a vestibularrelated cortical area, that is the right insula, underlying the effect of gravitational and vestibular deprivation. Also a decrease in cerebellar-motor connectivity was found in astronauts after space flight which suggests that problems which arise after a space flight have both a central and peripheral causes. 20 The current study, however, suggests that several of these problems are because of modifications at the cortical level, and not merely because of peripheral neurosensory organs. These changes in brain function could explain the fact that second time flyers have lesser degree of these problems than first-time flyers, because of neural adaptation. The reversible problems after spaceflight discussed above have often been summed up because of apparent changes in vestibular system and in particular to the altered capacity of otolith system in sensing gravity. ²⁰

4.4. Neuroplasticity

Exposure to microgravity alters the sensory motor inputs. There is associated structural change in the brain. The CNS attempts to recalibrate the entire internal body system to be in synch with the external environment of outer space. This is partly achieved by Neuroplasticity. Neural plasticity or neuroplasticity can be defined as the capability of the brain to alter its structure or function in response to exposure to new stimuli or environments.

4.5. MRI & Advanced Imaging

Various analysis techniques such as BOLD connectivity measures which uses hypothesis-driven seed-voxel analyses or data-driven independent component analyses, amplitude of low-frequency fluctuation or ReHo measures have been used to study the dynamic properties of the human brain. ²¹

4.6. Functional MRI

Functional MRI investigation of brain function in a cosmonaut after 6 months in space microgravity shows changes in vestibular and motor-related regions. Reduced vestibular function and difficulty in motor control abilities at re-entry into earths atmosphere can be because of these changes. Understanding the effects spaceflights have on the human central nervous system is extremely important for to develop adequate countermeasures to prevent space flight related injuries.

The resting-state fMRI with low-frequency amplitude (0.01–0.08 Hz) fluctuation (ALFF) is a useful method to observe altered brain activities. ²²

Based on the results of this study, to maintain an adequate performance in microgravity, the use of dopaminergic agents may help to boost the brain functions in specific areas of brain.²³ The ALFF results comparing the normal

condition and a simulated microgravity condition are shown in Fig. 1 and Table 1. As compared to the normal condition, a reduced ALFF was observed in the left thalamus (including the medial dorsal nucleus and ventral lateral nucleus) in individuals spending variable time in a simulated microgravity condition.

The use of electro-physiological and neuroimaging techniques should be used to understand and analyse the structural, functional and metabolic changes that occur in central nervous system before and after a space flight. This can be done by use of high-density EEG, TMS and/or NIRS. This would give more comprehensive insight into spaceflight-induced neuroplasticity. Use of different techniques simultaneously may overcome limitations because of use of one single technique. For example combining EEG and MRI would give a more detailed findings of the temporal dynamics and spatial information of the underlying neural processes taking place. ²⁴

4.7. Radiation effects

Radiation is measured in millisieverts (mSv). On Earth, exposure to 2.4 mSv is normal. Readings above 100 mSv, are more likely to be carcinogenic. Astronauts and cosmonauts abroad International Space Station (ISS) sometime face levels of 200 mSv, and occasionally interplanetary levels of radiation are around 600 mSv. Researchers speculate that travel to Mars could involve a 30% increased risk of cancer because of exposure to increased doses of radiation. Cosmic rays, or high-energy, ionizing cosmic ray (HZE) nuclei, are a form of space radiation not experienced by inhabitants on Earth. They are usually absorbed as radiation travels through various layers of earths atmosphere or deflected by Earth's magnetic field.

One particle, it is theorized has the power to charge through human tissue and causes changes at a very genetic level raising the risk of mutations subsequently leading to cancer. Cosmic radiation may also cause disorders of the central nervous system.

Setlow explains that metals, including lead and aluminum, do not offer much protections in deep space, and they would be heavy and cumbersome. He recommends use of water or plastics in the future. Other ideas include a plasma shield, confined by a magnetic field, to absorb and reduce the potential carcinogenic effects of incoming particles. ²⁵

The basic aim of human space-flight programs is to continue the exploration and development of deep space along with minimizing the various risks from exposure to ionizing radiation. Astronauts are considered as radiation workers and as of now follow the "as low as reasonably achievable" principles and guidelines, along with radiation monitoring to document exposure. NASA and the other international partners have been analyzing and applying the recommendations of the National Council on Radiation

Protection to reduce the radiation exposure to humans during space-flight. ²⁶

4.8. Mobile health technology

Mobile health Technology (mHealth Systems) is poised to find extensive use in outer space missions. The various applications and services supported by mHealth systems include:

Mobile telemedicine including use of remote consultations, detailed storing of patient data.

Also personalized monitoring of vitals which is achieved through interconnectedness with wearable devices.

Location-based medical services to ensure delivery of locally-relevant information Emergency response and management, along with regular access to health care information.

5. Conclusion

The Brain is known to constantly adapt itself to the external environment. Prolonged exposure to microgravity poses a formidable challenge to the neural network. So far lot of information exists about neuroscience in outer space. More studies are required in this unchartered field. Understanding the complex neurophysiological changes and its interplay with outer space can provide important insights to device counter measures and chalk out treatment modalities for the deleterious effects due to microgravity and radiation. As numbers of Vyomanauts and space tourist increase in future, there will be an inescapable requirement to provide health care in outer space travellers. At present it, seems to be a tall order but, not impossible.

6. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

7. Source of Funding

None.

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