Neurophysiology of Space Medicine: A Literature Review

Jose R. Velasquez
The University of Texas Rio Grande Valley, jose.velasquez@utrgv.edu

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Abstract:

Space medicine is becoming an essential and expanding clinical discipline. Acquiring a deeper and complete picture understanding of the multi-systemic response due to space on human health and function is essential to ensure the success of future space exploration. A comprehensive review of the literature was performed using PubMed and focused on the current neurophysiologic findings of the central nervous system's response to space. Ground-based analogues, which mimic the effects of microgravity, and actual spaceflight studies have been used to analyze these physiologic adaptations to space. Overall, cerebellar, sensorimotor and vestibular brain regions seem to be affected the most. Through these and future studies, the goal should be to extend the distance that humans go into space and to increase the time that they can stay there.

Introduction:

With plans from NASA to send humans to Mars by the 2030s and SpaceX's mission of making humanity multiplanetary through their fully reusable launch vehicles, space medicine is becoming an essential and expanding clinical discipline that will ensure the safety and success of future space endeavors. From the physiological and adaptive changes of the human body due to microgravity and radiation to the psychological challenges of isolation and confinement, it is important to acquire a deeper and complete picture understanding of the multi-systemic response due to space on human health and function. While advancements in the cardiovascular and musculoskeletal responses to spaceflight and microgravity have been well-documented, advancements in nervous system responses, specifically the central nervous system (CNS), have not progressed as rapidly until recently. While it is important to understand the CNS response in order to develop new and optimize current health countermeasures, it is more so important to understand these responses in order to maintain the high level sensorimotor and cognitive processes needed to complete the many critical tasks for a successful space mission. From ground-based Earth studies to spaceflight studies, this literature review will serve to summarize the current neurophysiologic MRI findings of the central nervous system's response, specifically of the brain, to space.

Materials and Methods:

A comprehensive review of the literature was performed using PubMed. A set of Mesh terms were used as follows: (("Aerospace Medicine"[Mesh]) OR ("Space Flight"[Mesh]) OR ("Astronauts"[Mesh]) OR spaceflight OR "space flight" OR astronaut* OR "space medicine" OR aerospace) AND ((neurophysiology) OR (nervous system) OR ("Neurophysiology"[Mesh]) OR "Nervous System Diseases"[Mesh]). No language restrictions were enforced; however, date restrictions were set from 2015 to 2020 due to the lack of studies published in 2021. Articles chosen will be of ground-based MRI studies of the brain and pre- and post-spaceflight MRI studies. Articles were also chosen based on findings particularly pertaining to the brain. A list of articles was organized using a Word document and studies that showed similar findings were not included.

Results:

This search criteria yielded 1,308 results and each resulting articles were examined for potential relevance. After careful consideration, 7 articles were selected due to their direct relevance to neurophysiologic adaptations of the central nervous system to spaceflight.

Discussion:

Some of the studies pertaining to the physiologic adaptations to space come from ground-based analogues, which mimic the effects of microgravity. These space analogues include parabolic flights, dry immersion, and the most implemented, head-down bed rest (HDBR). In head-down bed rest, a subject lies in a bed that is inclined with the head down for a week, a month, or longer, which replicates the space-induced cephalic fluid shift. The restriction to the bed also mimics the immobilization and isolation experienced in space.

Through HDBR, particular attention on the central nervous system has been put on neural plasticity. This is due to the thought that cellular and molecular changes can result in structural effects detectable with MRI. MRI is a high-resolution neuroimaging technique used to investigate cortical activation patterns and allows detailed assessment of the structural and functional connectivity of the brain (Zatorre et al. 2012). Of note, the brain is composed of two primary tissue types: gray matter and white matter. Gray matter is composed of neuron cell bodies and glial cells. It is responsible for modifying and collecting information transmitted from nearby neurons and from distant areas via bundles of myelinated axons known as white matter tracts.

Dynamic and major structural brain changes have been particularly observed through volumetric grey matter changes in sensorimotor brain regions such as the primary motor cortex, somatosensory cortex, and the cerebellum. These brain regions are responsible for planning, control and execution of voluntary movement, sensorimotor coordination, and processing sensory inputs (Koppelmans et al. 2017). Moreover, HDBR lead to changes in balance and functional movement performance as seen by volumetric grey matter changes in a cluster that compromised the precuneus, and pre and postcentral gyri. These brain regions are responsible for sensory perception, motor control, and mental orientation in space, time, and person. It is important to note that larger volumetric increases in grey matter were associated with smaller declines in balance (Koppelmans et al. 2017). Thus, structural changes in these regions could potentially affect the functions controlled by these regions. These structural changes may include dendritic branching, synaptogenesis, axonal sprouting, changes in glial number and morphology, and angiogenesis. It is proposed that changes in grey matter plasticity is due to a response to the altered sensory inputs presented to subjects as a result of HDBR. However, it is also suggested these gray matter changes were due to headward interstitial fluid shift related to the increased intracranial pressure and fluid redistribution caused by HDBR (Koppelmans et al. 2017). Furthermore, HDBR also caused upward and posterior brain shift, increased density of brain tissue at the vertex such as the central frontoparietal lobes, contraction of adjacent extra-axial cerebrospinal fluid spaces, and increased ventricular volume (Roberts et al. 2015). These changes are hypothesized to result in changes in cerebrospinal fluid flow dynamics and compression of the dural venous sinuses along the vertex, resulting in venous outflow obstruction and increased intracranial pressure.

While ground-based analogues circumvent the logistical and financial restrictions of studying the central nervous system changes in space, the method of using MRI studies of the brain before and after spaceflight has been implemented. One of the first findings of changes in brain connectivity was decreased connectivity within the right insula, an area involved in vestibular processing and cognitive control. These findings highlighted the effect of gravitational and vestibular deprivation. Decreased connectivity between the motor cortex and cerebellum was also observed (Demertzi et al. 2016). Long duration space flight resulted in narrowing of the central sulcus, an upward shift of the brain and narrowing of CSF spaces at the vertex. CSF outflow obstruction may have also been caused by the rotation of the cerebral aqueduct, which was present in all long-duration spaceflight astronauts, and subsequently also caused enlargement of the ventricular system (Roberts et al. 2017). In addition, increased white mater volume was seen in the cerebellum, corticospinal tract, and primary motor cortex immediately after spaceflight. These results suggest that spaceflight induces these changes in the motor and coordination regions of the brain (Jillings et al. 2020). Sensory regions important to vestibular and proprioceptive processing also experienced changes post-spaceflight. Specifically, these areas included the inferior cerebellar peduncle, which serves to transmit information between the vestibular receptors and the cerebellum, and the right inferior and posterior parietal lobe, which integrate vestibular and proprioceptive information and play a role in perception of the spatial and upright representation of the body (Lee et al. 2019). Moreover, white matter changes were seen in areas related to vision and visual processing, specifically the superior longitudinal fasciculus, which is important for visuospatial processing, visual attention, and visuomotor control, and in the inferior longitudinal fasciculus and inferior fronto-occipital fasciculus, which may play a role in visual recognition, visual processing, visually guided decision making, and language comprehension (Lee et al. 2019). Changes in white matter tracts involved in motor function were also observed including decreased organization in the corticospinal tract and the primary motor cortex. Lastly, white matter alterations were also observed in the middle cerebellar peduncle, which is a region that facilitates initiation, timing and planning of movement through its cortico-ponto-cerebellar tract (Lee et al. 2019).

The major limitation of neuro-imaging studies in spaceflight and ground-based analogue subjects is due to the small sample sizes. This leads to limitations in the ability to use statistical models necessary to determine significance. Moreover, these studies are limited by the fact that currently there is no way to analyze spaceflight associated brain alterations in flight, as MRI can only be performed on Earth. Lastly, the sparsity of neuroimaging data on female astronauts is another limitation of these studies and should be addressed in future studies given the plans to send both men and women on future long-duration space missions.

Conclusion:

This review summarized the most recent findings of neuroimaging-evaluated changes to the central nervous system, specifically the brain, after spaceflight and ground-based analog studies, specifically HDBR. These recent advancements highlight the immense scientific effort to develop a deeper understanding of the impact of spaceflight on multiple central nervous system regions that result in structural and functional changes. Overall, cerebellar, sensorimotor and vestibular brain regions seem to be affected the most. Further studies will guide the development of certain countermeasures that would aid in improving these adaptive effects of the central nervous system and ensure the preservation of sensorimotor and cognitive performance necessary for successful spaceflight missions. Further studies are also needed to keep identifying, monitoring, and mitigating potential maladaptive neurological changes as the goal should be to extend the distance that humans go into space and to increase the time that they can stay there.

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