Aerospace Medicine – An Evolving Field to Mitigate and Treat Organ Dysfunction Partly Caused by Premature Aging in Low Microgravity

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Abstract

Space medicine is a branch of aerospace medicine, which is a crucial field, albeit with minimal research. Research at the International Space Station and other endeavors has provided insights into how loss of gravity could affect the physiological functions of humans. Organs such as the heart could begin to deteriorate with lack of resistance from the planet. The musculoskeletal system, which is the anatomical backbone, may struggle to support the individual's structure. The cardiovascular system will be inefficient with respect to circulation, leading to other organ dysfunction. Radiation in space, also known as cosmic radiation, is caused by many different celestial bodies such as stars, sun, supernovae, and black holes. The Earth's magnetic field is a crucial component to protect humans from harmful radiation. However, once humans venture beyond the protective confines, the body becomes exposed to dangerous elements that pose a significant threat to safety. Living in microgravity also has detrimental effects on organisms' brains. These include but are not limited to sustained effects on circadian rhythm, emotional dysregulation, and cognitive dysfunction. This article discusses the threat of

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premature aging during long- and short-term times in space due to high risks associated with space travel. Improvement of clinical intervention is hindered by a lack of research and development, which is needed to fundamentally address these risks.

Keywords: Aerospace medicine, immune aging, nephrology, psychology, radiation, hematopoiesis.

Introduction

A common misconception that people have is that only governmental agencies, such as the National Aeronautics and Space Administration (NASA) and the European Space Agency (ESA), are the sole entities to conduct research and send humans and other organisms to space [1]. Several private entities have emerged recently that adds to what is ongoing with governmental sectors. These include but are not limited to SpaceX, Virgin Galactic and Sierra Space. These companies have started to participate in the research space and to be involved in the economic aspect for long-term space habitation [2–4].

Aerospace medicine, similar to space tourism, could be considered as nascent but emerging fields. The Department of Space Medicine created by the US Air Force was initiated in 1950 and represents one of the first federally owned agencies. The main goal was to increase humanities by knowledge of the human body's response in the absence of Earth's gravity. The research typically focuses on the well-being and safety of an individual in air and space travel. Aerospace medicine has several areas of concentration, each focused on a specific aspect of care. These include research, operational support, safety, and patient care of the passengers within space vehicles [5]. It is a challenging field as multiple considerations of variables aside from traditional patient care are necessary. These include challenges caused by lack of gravity, G-forces, acceleration, radiation exposures, and high-altitude conditions. New innovations have been made to reduce premature aging in space which can be caused by living in microgravity [6].

Inventions such as artificial gravity, and gravity exercise machines, could make long-term space missions comfortable and safe for astronauts [7, 8]. Spaceships carry humans and other organisms with the goal of understanding the effects of microgravity on human body and experimental systems. These effects were compared with baseline functions while on Earth when the human and organisms are adjusted to the comfort of gravity [9, 10]. A meaningful study sent one twin to space for a year, and the other twin remained on earth [11]. Up to this time, humans spent less than 300 days space with a few reports of astronauts spending >300 days [11, 12]. Thus, it was remarkable that a single set of monozygotic twins were able to provide great insights into the physiological outcome of low gravity without confounds by varied MHC-II for a 1-year stay in space [12].

A close review of clinical parameters reported for the twin in space point to a case of premature age [12]. One can argue that perhaps this astronaut was already at middle age and began the process of natural aging. However, when compared to the identical twin, is telomere is shortened, decrease bod mass and DNA damage, among others [12]. Timeline showed some improvements. However, the long-term effects are yet to be discerned. Interestingly the changes in microbiome could be reversed. However, the long-term effects of such changes are yet to be elucidated since the microbiome of the gut could influence organ functions including neural behavior [13]. Going forward, using human to study physiological changes by low gravity requires ethical discussions. It is important to include bioethicists in these decisions.

In general, astronauts have spent relatively short time in space for drastic physiological evolution to be discerned. This short time might allow for organ adaptions by the cardiovascular, musculoskeletal, and the sensorimotor systems. To counteract the untoward effects of living in microgravity, astronauts endure a rigorous exercise schedule. However, as the study showed that some of the protocols may not have been fully effective in preventing absolute negative impacts of long-term spaceflight on the musculoskeletal system. While exercise may be useful, such intervention might not be adequate for the premature aging caused by low gravity.

If one equates short-term stay in space as safe, this is likely to be misleading. We discuss this point by examining the gap to study young humans who have been exposed to insults by surgical trauma, cancer and perhaps psychological stress. Immediate follow-up of clinical tests could deem these individuals as healthy and without aging disorders. However, this might not be the same in a few years, long before their biological age. It is likely that these individuals could undergo premature aging. Similar occurrences could be the same for short-term space flight underscoring a need for outcome research on these individuals.

Gravity of Earth Versus Other Planets

It is critical to comprehend the distinctions between space and Earth to appreciate the significance of aerospace medicine. A rapid evaluation of these differences might appear to be few. However, these changes are prominent to cause major life-changes. The report indicated that one astronaut lost his vision while in space by a phenomenon referred as SANS (Spaceflight-Associated Neuro-Ocular Syndrome) [14]. Furthermore, astronauts are susceptibility to increased presentation of cancer and cataracts after prolonged stay in space [14]. SANS is a common effect of astronauts who were on the International Space Station (ISS) [15]. Subjects experience swelling in the back of the eye resulting in temporary loss of vision.

Earth's unique mass and gravitational forces has forced organisms to adapt and combat the resistance due to gravity. If taken to other planets, such as Jupiter or Saturn, the organism's body would have challenges to handle pressure. The field of aerospace medicine is intended to ease the transition from earth's gravity to another celestial object's gravity.

Radiation Exposure in Space

Exposure to radiation in space, referred as 'space radiation', increases the risk of astronauts to develop cancer. Preventive measures of radiation exposure include shielding that would absorb radiation. In the case of space radiation, this often includes creating materials out of special polymers and devising electric/magnetic fields to block radiation particles. Earth has a natural magnetic field that can diminish the major effects of space radiation exposure on astronauts. Regarding travel outside of Earth's protection, radiation exposure becomes a major area of concern. An understanding of morbidity risk and toxicity associated with space radiation remains limited. Despite a large body of literature on the effects of anticipated radiation doses, there is a lack of detailed and concrete calculations due to the complexities of the radiation environment, shielding effects, limitations on areas further than the Earth's magnetosphere, and variations in human anatomy. Furthermore, knowledge of basic mechanisms related to low-dose radiation, sequential doses, and adaptive responses is still in its early stages. In-depth research studies with comprehensive omics approaches may provide clues into the instability and delayed mutagenesis in place with space radiation. This will aid in assessing risks associated with potential space radiation-induced degenerative diseases.

Musculoskeletal System

The musculoskeletal system consists of bones, muscles, cartilage, tendons, ligaments, and joints. It is an intricate system that allows our body to be able to move within our environment, provide support and protection for our vital organs, and even generate heat. Bones have many special properties with constant reshaping in response to stress, such as exercise. On Earth, gravity applies a constant load to the musculoskeletal system, which causes healthy bones to maintain physiological bone density that allows humans to remain mobile and participate in activities of daily living. But living in space drastically affects the musculoskeletal system. Bone loss occurs in the weightless environment of space because bones do not need to support the body against gravity. In short-term travel, the effects of microgravity on the bones are relatively minor [16]. One of the major obstacles to long-term space missions is the threat of severe bone loss in astronauts. Decreased bone mass, called osteopenia, leads to an increased likelihood of changes that weaken skeletal integrity and an increase in the rate of fracture injuries [1]. This raises an important issue as we do not know how long-term space travel may affect bone remodeling and density. Aside from the effects of microgravity, the exact mechanisms and cellular signaling pathways by which alterations occur are in bone, cartilage, tendon, ligament, and connective tissue. Despite the development of drugs and treatment regimens for decreased bone mass and density, these treatments have only been tested on Earth. The use of long-term, extensive use of therapeutics (such as osteoporotic drugs) has yet to be studied in long-term space travel. This may produce potentially serious adverse effects in a microgravity environment.

Cardiovascular Impact

The basic unit of cardiac muscle are cardiomyocytes [17, 18]. Encouraged research in space has become valuable tools, including studies that ship cells to space [17]. It is postulated that changes in cardiomyocyte gene expression may arise from microgravity conditions or radiation exposure and thus must be investigated when considering long-term space missions/travel [17]. The experimental evidence suggested effects on the heart's electrical conduction system [18]. Specifically, there may be changes in the sequence of the impulses responsible for the synchronized contraction of the heart's chambers that allows for systemic blood flow. Cardiac arrhythmias cause the heart to pump less effectively, increasing the risk of clot formation, decreased perfusion, and blood flow to the organs. This, in turn, raises the risk of sudden cardiac death, stroke, cardiovascular disease, and even dementia. While certain studies suggest the impact of space travel on heart electrical conduction is multi-faceted, there has been an association with certain forms of arrhythmias (QT Prolongation) on longer flights [19].

Psychological Impact in Space

The challenges faced by astronauts extend beyond physical risks and encompass significant impacts on their mental health [20]. These areas include emotional dysregulation, cognitive dysfunction, and disruption of sleep-wake rhythms. The impact on the circadian rhythm is profound: for each 24-hour Earth Day, astronauts on the International Space Station see 16 sunrises and sunsets [1].

Artificial light on the station is largely made up of a specific wavelength of blue light, the same blue light that is used by cell phones and television screens. This blue light tricks the body to stay awake, instead of going to sleep. These factors in tandem may contribute to long-term sleep loss. People who consistently lose sleep tend to have decreased executive function or the set of mental processes involving concentration and decision-making, visual phenomena, changes in body weight, and morphological brain changes, are common occurrences during space missions [21]. Countermeasures, including emotional training and psychological support, are crucial for mission success. The challenges continue upon the astronauts' return to Earth, requiring careful consideration for their mental well-being during the reintegration process.

Other Age-related Considerations

We and others have determined that young factors can influence aging disorders [22–24]. Experimental outcome in space research supported increased oxidative stress, inflammation and altered mitochondrial functions [25]. Since immune cells are generated in the bone marrow, an understanding of this organ in space could explain immune dysfunction. The increased inflammation and oxidative stress are reminiscent of age-related hematopoietic dysfunction [26]. Since astronauts might be less or equal to middle aged individuals, low gravity could induce premature aging. Return to earth could show normal peripheral blood counts. However, this does not eliminate chronic hematological aging. We propose that methods to reset the aged hematopoietic system is required for individuals venturing in space. Studies with humanized mice showed that this is feasible and that the reset is stable [22]. Since a competent immune function could influence other organs, focusing on the hematopoietic system could be a benefit [27].

Perspective

The increase in space travel will require more robust research studies to understand how aerospace travel affect human physiology as well as the structure. While we have begun to understand the effects, most treatments have focused on astronauts who have undergone intensive training for months to years and are often in highest physical condition. Even with the available data discussed in this review, there is a need for additional studies, including methods to halt premature aging. This will provide a safe path for long-term space travel [28, 29]. Current research focuses on the early post-flight period, narrowing to immediate recovery post-travel. The key missing component is

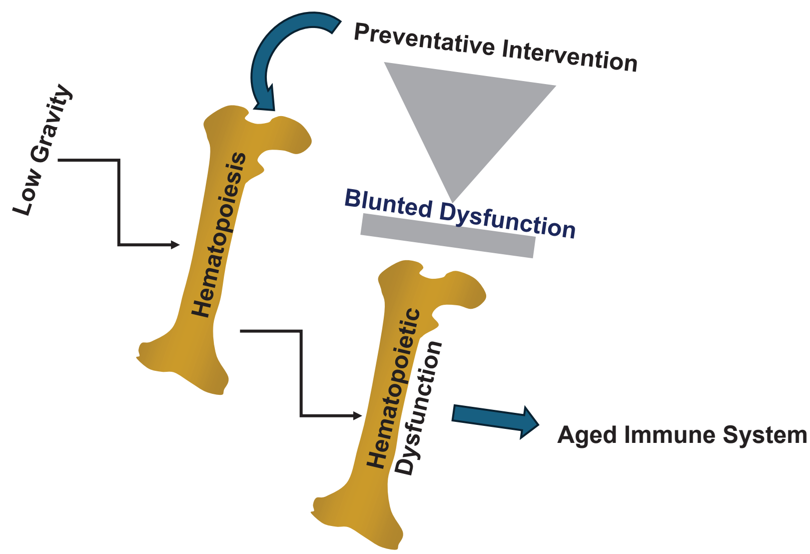

Figure 1 Cartoon shows gravity-induced hematopoietic dysfunction resulting in aged immune system. Shown is the possibility to establish non-invasive method to prevent dysfunction while in space. This will sustain the immune function in space for ease when returned to earth.

long-term surveillance and follow-up. Future research will result in positive outcomes to mitigate detrimental effects to life caused by microgravity. Overall, we propose that methods to prevent hematopoietic dysfunction in space could prevent immune failure (Figure 1). The experimental studies thus far indicate that it would be possible to establish a non-invasive method for preventive methods, in addition to reversing the change in the hematopoietic system.

This review did not address details of kidney changes due to the complexity of changes that could affect functions. However, experimental studies have provided insights of organ changes [30]. Studies with rats indicated differences in fluid balance between space and earth. During the early phase of space flight, there is a transient increase in glomerular filtration rate, independent of renal plasma flow. It appears that the kidney might have two phases of adaptation in space. It is unclear of these phases can be adjusted for adaptation.

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