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REVIEW ARTICLE

BRAIN IN SPACE. HOW DOES SPACE AFFECT THE HUMAN BRAIN?

MÓZG W KOSMOSIE. JAK WARUNKI KOSMICZNE WPŁYWAJĄ NA LUDZKI MÓZG?

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ABSTRACT

Introduction

Nowadays more and more people and international companies are interested in Human Spaceflights.

Aim and method

In this review, the negative effects from space radiation, microgravity and the factor of isolation on the central nervous system will be described in relation to space neuroscience and the relevant studies examined.

Results

Space radiation can damage neuronal connections with both acute and chronic effects, manifested as altered cognitive function, reduced motor function, and behavioral changes. Moreover, some astronauts report a condition known as Spaceflight Associated Neuro-ocular Syndrome (SANS). The brain scans performed upon those astronauts, who came back from space travel suggest that due to reduced gravity conditions the brain and the fluids in the human body shift upwards, which increases pressure in the skull and may result in optic-nerve swelling that causes blurred vision. Another interesting part of space neuroscience is the research of structural neuroplasticity. A study conducted on cosmonauts revealed an increase in the neuronal tissue of sensorimotor structures responsible for movement coordination. In addition to the space radiation and microgravity, long-term confinement also affects the microstructure of the brain white matter, which was proven in the study that used DTI (Diffusion Tensor Imaging).

Conclusions

To conclude, to continue understanding the risks posed by spaceflight to astronauts' health research in the field of space neuroscience is important. In addition, the acquired insight could be relevant for terrestrial vestibular patients, patients with neurodegenerative disorders, as well as the elderly population, coping with neurological deficits.

Keywords: space medicine, brain, space neuroscience, SANS, space radiation.

STRESZCZENIE

Wstęp

Współcześnie coraz więcej osób i międzynarodowych instytucji interesuje się załogowymi lotami w kosmos.

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Cel i metoda
W niniejszym przeglądzie negatywne skutki promieniowania kosmicznego, mikrograwitacji i czynnika izolacji na ośrodkowy układ nerwowy zostaną opisane w odniesieniu do neuronauki kosmicznej i przeanalizowanych badań.

Wyniki
Promieniowanie kosmiczne może uszkadzać połączenia neuronalne, powodując zarówno ostre, jak i przewlekłe skutki, objawiające się obniżonymi funkcjami poznawczymi, zmniejszonymi funkcjami motorycznymi oraz zmianami behawioralnymi.

Co więcej, niektórzy astronauci zgłaszają stan znany jako Spaceflight Associated Neuro-ocular Syndrome (SANS). Badania obrazowe mózgu wykonane wśród astronautów, którzy wrócili z kosmosu, sugerują, że z powodu zmniejszonej grawitacji mózg i płyny w ludzkim ciele przesuwają się w górę, co zwiększa ciśnienie śródczaszkowe i może powodować obrzęk tarczy nerwu wzrokowego, a w efekcie niewyraźne widzenie.

Inną interesującą częścią neuronauki kosmicznej są badania nad neuroplastycznością strukturalną w trakcie lotów kosmicznych. Badania przeprowadzone u astronautów wykazały wzrost tkanki neuronalnej w zakresie struktur sensomotorycznych odpowiedzialnych za koordynację ruchu. Oprócz promieniowania kosmicznego i mikrograwitacji, długotrwała izolacja wpływa również na mikrostrukturę istoty białej mózgu, co zostało udowodnione w badaniu z wykorzystaniem DTI (Diffusion Tensor Imaging).

Wnioski
Podsumowując, aby dalej rozumieć zagrożenia, jakie loty kosmiczne stwarzają dla zdrowia astronautów i zapewnić bezpieczeństwo oraz powodzenie misji, ważne są badania w dziedzinie neuronauki kosmicznej. Ponadto nabyta wiedza może mieć znaczenie dla pacjentów z zaburzeniami przedsionkowymi i neurodegeneracyjnymi, a także populacji osób starszych, zmagających się z deficytami neurologicznymi.

Słowa kluczowe: medycyna kosmiczna, mózg, neuronauka kosmiczna, SANS, promieniowanie kosmiczne.

Introduction

Space medicine is a branch of science that studies the effects of space conditions on human physiology. Due to research conducted within space medicine, we know today how space conditions affect living organisms, how humans adapt to such conditions, and how to prevent the negative effects of travel to outer space (Hodkinson *et al.* 2017).

Specialists in this branch of medicine are trying to find solutions that enable humans to survive and thrive in space. Space is a completely new environment for Homo Sapiens, full of challenges such as reduced gravity, cosmic rays, and conditions of isolation and confinement (Hodkinson *et al.* 2017). Given the growing interest of space agencies and private companies in sending humans beyond the Earth's orbit – to the Moon or Mars – and the coming era of Civilian Spaceflight (Stepanek *et al.* 2019) recognizing and countering threats will be essential to keep astronauts alive. So far, much is known about the effects of microgravity on muscles (Tanaka *et al.* 2017), bones (Grimm *et al.* 2016) and the cardiovascular system (Hargens and Richardson 2009). What is more, research on this topic is also carried out on Earth in the so-called analogs (Pandiarajan and Hargens, 2020), such as bed rest studies or during analog space missions, where the impact of isolation (Choukér and Stahn, 2020) in a small group on the well-being and behavior of crew members are tested. However, relatively little attention has been paid in research to the central nervous system, which is after all responsible for most of human actions and decisions. Hence, in the following publication, we have collected basic information on the effects of cosmic rays, microgravity and isolation on the central nervous system and the resulting consequences based on accessible data.

Space radiation

So far, space radiation is probably the most dangerous factor for human health in space, regarding the lack of sufficient countermeasures against it (Chancellor *et al.* 2014; Cucinotta *et al.* 2018). The space environment beyond low Earth orbit (LEO) poses the risk of exposure to several types of ionizing radiation among which galactic cosmic radiation (GCR) (Wiedenbeck, 2013) will contribute significantly to the dose accumulated by astronaut crew members. GCR ions contain highly energetic protons and alpha particles that can penetrate the hull of a spacecraft and tissues of the body producing complex lesions (Chancellor *et al.* 2014).

Primary biomedical risks that may pose significant health concerns for astronauts exposed to the radiation environment have been identified by The National Aeronautics and Space Administration (NASA). These risks include carcinogenesis (Cucinotta *et al.* 2018), degenerative tissue effects (Huff, 2009), acute radiation syndrome (Carnell *et al.* 2009) and CNS decrements (Cucinotta *et al.* 2009).

Of particular concern is the potential for radiation to influence critical decision-making during routine activities onboard or under emergency conditions in space. Studies conducted by Parihar *et al.* demonstrated the adverse effects of space radiation on cognition and linked them to the injury of neuronal structure and synapses in specific regions of the brain (Parihar *et al.* 2015). Furthermore, Parihar *et al.* showed that rodents exposed to cosmic radiation present persistent decreases in cognitive performance and impaired spatial, episodic and recognition memory, as well as increased anxiety. The irradiation caused a significant reduction in dendrite density and altered morphology of the prefrontal cortex and hippocampal neurons known to be involved in the behavioral tasks tested. Cosmic radiation also caused an increase in active microglial cells in the surrounding synapses. This phenomenon leads to the inflammation of the nervous system that lasted more than 6 months after exposure. The chronic neuroinflammatory process is presumed to reduce hippocampal neurogenesis, and thus to cognitive decline (Parihar *et al.* 2016). Structural changes were also temporally coincident with increased postsynaptic density protein 95 (PSD-95) known to decrease branching of primary dendrites (Charych *et al.* 2006).

These data come from animal models, however, studies conducted on patients undergoing head radiation therapy show a similar relationship. In addition to the above-mentioned mechanisms of action, the authors of one of the papers propose another, namely that ionizing radiation damages the vessels supplying the brain, which leads to ischemia and secondary white matter necrosis. Functional deterioration occurs most often in the areas of attention, information processing, and memory, and can lead to additional symptoms such as ataxia, urinary incontinence, and dementia (Lynch, 2019).

So, given the long-term effects of space radiation on neuronal structure, neuroinflammation and synaptic protein levels, it is hard to imagine how these collective processes would not negatively impact astronauts' neurotransmission, cognition, well-being and behavior. The radiation environment in deep space could be problematic for astronauts and their capability to efficiently operate throughout travel and can impact the success of a mission.

Microgravity

The problem of redistribution of body fluids under microgravity conditions affects all organ systems, including the central nervous system (Hodkinson *et al.* 2017). Research in the field of space neuroscience has been focused on the vestibular system and sensorimotor deficits that include spatial disorientation, impaired gaze control, reduced fine motor control and postural ataxia (Bloomberg *et al.* 2015). Astronauts gradually adapt their sensorimotor processing during space missions in response to body unloading and altered vestibular inputs. This adapted sensorimotor state is then inadequate upon return to Earth's gravity conditions because astronauts show slow re-adaptation over days and even weeks postflight (Mulavara *et al.* 2010).

However, significant structural changes within the brain after spaceflight were also reported and included narrowing of the central sulcus and increased volume of ventricles, an upward shift of the brain and twisting of the cerebral aqueduct (Donna R. Roberts *et al.* 2017). Long-term stay in space is associated with an increase in the total volume of the brain and cerebrospinal fluid (CSF). Additionally, increased ventricular volumes in astronauts persisted elevated at 12 months post-flight (Kramer *et al.* 2020).

Increased intracranial pressure may cause swelling of the optic nerve and a change in the shape of the eyeball, which manifests in Spaceflight-Associated Neuro-ocular Syndrome (SANS). The intracranially accumulated CSF resides in spaces such as the ventricles, but if these spaces are maximally expanded, CSF might build up in the retro-orbital space eventually leading to signs of SANS. Clinically, astronauts report blurred vision and degradation in distant and near visual acuity, some of which remain unresolved years after flight. MRI examinations of cosmonauts returning to Earth show excess fluid behind the eyeball that causes swelling of the optic nerve disc. What is more, some authors even proved that larger visual acuity decreases in cosmonauts postflight are associated with larger brain ventricular expansions (Jillings *et al.* 2020). On the other hand, Roberts and colleagues (Roberts *et al.* 2019) found that astronauts reporting symptoms of SANS showed smaller increases in ventricular volume compared to those who did not develop SANS. These seemingly contradicting findings highlight the need for more research in a larger group of individuals to address the link between SANS and redistribution of body fluids and changes in brain tissue. Such data might be used as biomarkers useful to predict the occurrence of SANS. Moreover, it is worth mentioning that most of the SANS cases are reported by NASA astronauts, while it has been claimed that SANS does not develop in Roscosmos cosmonauts. This difference may come from varied countermeasure schemes used among the space crew populations (Jillings *et al.* 2020).

Except for SANS, there is also another point of interest in terms of structural changes in the brain in space. One of the newer studies focused on the phenomenon of neuroplasticity showed how the human brain adapts to microgravity conditions. Magnetic Resonance Imaging (MRI) scans performed on cosmonauts showed an increase in nerve tissue in the basal ganglia and in the cerebellum, so structures responsible for motor coordination, maintaining balance, spatial orientation, and precise movements. Interestingly, these changes persisted even 7 months after returning to Earth (Jillings *et al.* 2020). Taking into account the functional and behavioral implications, understanding these effects on the grey matter (GM) and white matter (WM) is crucial. Structural neuroplasticity presented in this study is likely to be considered as an adaptation of cosmonauts' brains' motor strategies to the microgravity environment and readaptation to the conditions on Earth after the flight. Changes observed by Jillings *et al.* are not likely to have a negative clinical impact on the health of the cosmonauts but rather reflect positive adaptations. Perhaps this phenomenon explains why experienced astronauts adapt to space conditions much faster than those who are exposed to them for the first time.

Isolation and confinement

Another challenge that the spaceflights crew faces is isolation and confinement. This further results in mental health issues as well as in changes in the brain microstructure (Brem *et al.* 2020).

The environment of the spaceflights is what has a major influence on the mental health of astronauts. This is by some indicated as one of the main problems that long-distance space flights crew must face (Slack *et al.* 2016). The emerging problems result from, among others, circadian rhythm changes, interpersonal contacts issues among the crew members and separation from family and friends. The longer the isolation and confinement last, the higher the risk of developing mental health problems. This is a vital problem as the longer space travels are going to be more common.

Disorders such as anxiety, post-traumatic stress, sleep loss/insomnia, and depression can also occur unexpectedly in generally healthy individuals. Sensory deprivation and isolation in a constant, unchanging environment can cause hallucinations or optical illusions. The problem may seem trivial in the context of the ISS mission, but when we think about traveling to Mars and living there, it seems that this may be one of the most important challenges to think about.

Psychopathologies in space can be a direct threat to life. When we think of conditions that require immediate medical attention, we usually think of trauma, heart attack, head trauma, or acute appendicitis. Any of them can, of course, happen in space, but apart from injuries, the second most common medical cause requiring evacuation during submarine missions (space mission analog) were psychiatric disorders (Ball and Evans, 2001). Among other conditions, depression and anxiety were the most common psychiatric diagnoses during these missions and were also common among researchers working in Antarctica (Lugg, 2000). Stressors related to confinement in a small space include, among others, the lack of privacy and free movement, monotony and restrictions related to hygiene or nutrition (Suedfeld and Steel, 2000).

During a 520-day analog Mars mission which included 6 individuals, 4 out of six indicated sleep pattern disturbances at some point of the study, and one of them developed symptoms of mild depression as indicated by the Beck Depression Inventory – Second Edition (BDI-II questionnaire) (Basner *et al.* 2014). However, Alfano *et al.* in their 2018 paper indicate studies in which there were no significant mood differences throughout the space flights and some in which some members of the crew developed positive emotions such as the sense of being accomplished (Alfano *et al.* 2018).

Isolation and confinement have been proven to have an impact on the brain microstructure. A study (Brem *et al.* 2020) performed among the crew of 520 days analog Mars mission represented significant changes to the brain using Diffusion Tensor Imaging (DTI). Fractional Anisotropy (FA) was significantly lower among the crew compared with the control. The changes were noticed in the following parts of the brain: anterior parts of the callosal body and the temporo-parietal-junction-zone of the right hemisphere. This shows that long-term exposure to the changes associated with stressors to which spaceflights crew is exposed may result in physical adaptations and changes to the brain. However, due to the small number of study participants, further research is needed to confirm these results and evaluate their consequences.

The authors studying mood changes and the phenomenon of adaptation to confinement and isolation pay attention to the behavior related to the "third quarter hypothesis" (the critical moment of being in isolation was the time constituting the third part of the entire mission) (Décamps and Rosnet, 2005). It was then that problems related to the relations between the crew members were identified (arguments, exaggerations, territorial behavior, withdrawal or exclusion of individual crew members and conflicts resulting from cultural differences) (Sandal *et al.* 2006; Kanas *et al.* 2001). All these phenomena will potentially be exacerbated during a long mission to Mars. Additional maladaptive reactions, such as sleep disorders, anxiety or depressive disorders, which will vary in intensity depending on individual characteristics, can also be expected (Basner *et al.* 2014). When planning a space mission, the psychological constructs of crew members should be taken into account to identify those who will best withstand the conditions of such a mission. Appropriate psychological tests and questionnaires should be used in the qualification process.

Conclusions

So, what does this all mean for a mission to the Moon or Mars and for space agencies' future plans for deep space exploration?

The analysis of the research on the impact of Space on human brains points clearly that the Central Nervous System is sensitive to exceptional space conditions such as space radiation, microgravity, isolation and confinement. All the consequences of exposure to the factors mentioned above may predispose astronauts to performance decrements, faulty decision-making and long-term neurodegenerative effects and, in consequence, affect the success of the space mission.

This impact should be taken into consideration especially before planning missions to Mars or deep space exploration expeditions by space agencies. As the plans for further and longer space missions appear, the greater the exposure to the negative effects of the space conditions will be. The research so far has been performed on a small number of individuals, therefore multidirectional research of space neuroscience is essential to understand the dangers for astronauts in space to ensure their safety in long-term missions. One of the solutions is to continue performing analog space missions, which would resemble the actual space conditions and would enable further explore the impact of isolation and confinement on the brain.

In addition, the insight obtained through analyzing the impact of space conditions on the Central Nervous System may be important for patients on Earth as well – patients with neurodegenerative disorders, as well as the elderly, struggling with neurological deficits. A similar situation has already taken place during research on bone loss in space – it contributed significantly to understanding the mechanisms that occur in the pathophysiology of osteoporosis on Earth.

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