EFFECTS OF MICROGRAVITY AND IONIZING RADIATION OVER HUMAN BODY (A REVIEW)

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Abstract

The current overview emphasizes on the physiological changes due to the combine effects of microgravity and ionizing radiation. Those two factors are significant to Astrobiology and our ambitions to travel into Space. The development of the technologies gives opportunity to combine and to make comparison between experiments carried out at real cosmic environment like the International space station (ISS) and ground ones, simulating the conditions of interstellar voyage. Experimental animals and cell cultures, representative for the specific system and organs, are used in those types of researches. Data obtained have traced many reliable findings: morphological and functional changes in neuronal tissues (expressed as decreased number of cells and change of their form), vascular system disorders (hemodynamics modulations, pulse rate and blood pressure alteration), and skeletal muscles weakness (change in volume and mass). Effects, due to ionizing radiation, are accelerating apoptosis and activating compensating mechanisms for oxidative stress. Both microgravity and irradiation by ionizing radiation are having combine effects in the cell cycles, genome mutations and apoptosis.

Keywords: *microgravity, weightlessness, ionizing radiation, random positioning machine (RPM), rat*

I. Introduction

The human species have survived on planet Earth and evolved by its curiosity. This is the main reason to have all technological advantages like computers, nuclear energy, rockets-etc. The latest is manifestation of „beyond horizon" imagination of human mind. Traveling in deep space is linked with many difficulties, including all stresses factors having impact on astronauts. These stresses include lack of gravity, physical and social isolation, lack of privacy, fatigue, and changing work/rest cycles [1]. Their impact on the human body can be observed taken alone or in combination.

The humanity has used to Earth's gravity. The whole evolvement of terrestrial organisms is subordinated to gravity. However, in space travel it must face microgravity. Exposure to weightlessness is associated with numerous problems like physiological disturbances, including cardiovascular deconditioning, bone and muscle loss, immune and metabolic disorders, visual/ ophthalmic aberrations, sensorimotor disturbances [2], redistribution of a fluid within the body [3] and neuronal changes.

Other factors affecting astronauts' condition are ionizing radiation (IR) and high-energy nuclei component of cosmic rays (HZE). Their impact on the human body is critical, even for the generations. Curtis et al [4] suggests possible 3-year-long mission to Mars, 13% of neurons in the CNS will be permeated at least once by an iron ion and at the same time ∼50% of neurons in the hippocampus will be hit by charged particles with an atomic number greater than 15.

However, it is very difficult to predict and pre-analyze all effects of space exploration due to the cost and danger. That is why scientists often use other methods to simulate those factors at ground-based experiments. For microgravity – hind limb unloading (HU, animal model), random positioning machine (RPM), parabolic flights, head down tilt (HTD) bed rest etc. It is commonly used accelerators and nuclear sources for simulation of IR and HZE.

1. IMPACT OF THE MICROGRAVITY

1.1. Effects of weightlessness on behavioral reactions

There are variety of tests to determine the behavioral actions with experimental animals. The most common used ones are Morris Water-Maze (MWM) [5], Open field test (OFT) [6], different type of maze (T-maze, Y-maze, Radial arm maze), etc. Anomalies are shown in the behavior of the animals under microgravity.

Wassersug and Izumi-Kuratani [7] have showed that reptiles in near 0G parabolic flight are obtaining behaviors that they show in 1-G under special circumstances. For example, snake is getting defense position and strike herself. Another study shows that mice on the board of ISS began to engage in a unique circling or 'race-tracking' behavior in which they moved their bodies along an ovular trajectory within 8–10 days post-launch [8]. Additionally, a notable decrease in socialization is observed among rodents used in space experiments, like stressful circumstances [9].

1.2. Effects of weightlessness on cognitive capacity

Changes in the cognitive capacity and memory can be crucial for space missions. However, there are controversial results in this area.

Reaction time is one of the parameters evaluating the cognitive condition. Short-term weightlessness can enhance reaction time in humans [10]. In another study, Temple et al. [11] show that changes in memory and learning are temporary due to microgravity. Observing the results, they suggest that Earth organisms can rapidly adapt to simulated changes in gravity. The reason for this may be cause of alterations in the morphology of neurons. In vitro studies, using mature neurons, demonstrated changes in alterations of the neurite network due to short- and medium-term exposures to simulated microgravity. However, these alterations were followed by fast recovery. Also, the long-term exposure to simulated weightlessness with RPM revealed a high level of adaptation of single neurons to the new conditions as well as a partial adaptation of the neuronal networks, that was concomitant to an increase in apoptosis [12].

On the other side, simulated microgravity in HDT bed rest may disrupt the function of right inferior frontal gyrus and left inferior parietal lobule in the resting state, which may contribute to changed abilities of mental transformation [13]. Keeping humans in prolonged weightlessness leads to problems in attention, spatial orientation and performance in tests of abstract thought [14]. Taken together, a combination of behavioral and biochemical experiments, a study demonstrates that simulated microgravity of more than 14 days-duration HU could damage the ability of learning and memory in rats. Those effects were accompanied by a significant increase in cholinergic dysfunction and oxidative stress [15]. Furthermore, simulated weightlessness cause more severe brain cortical damage [16].

1.3 Effects of weightlessness on skeletal system.

The importance of the astronauts' mobility is equal to their mental state for successful mission not only on the ISS, but to future ones to distant destinations like Mars. Effects of the microgravity over skeletal system can be observed in the bones, muscles and sensor motional functions.

Bones are "mechanosensitive", which in microgravity is causing changes in bone cell activity and results in a loss of bone mass [17]. There are several factors like reduction in mechanical load stimulus, reduced fluid pressures in the legs, and altered nutritional intake and metabolic processing that are having a combine impact over bones structure. Keyak et al [18] measured changes in bone strength that occurred during 4 to 6-month ISS missions. The results showed that the strength of the proximal femur decreased by 2.6% per month. Separately and in combination, HU and food restriction caused a reduction in total bone mineral density in proximal tibia metaphysis [19]. Those facts lead to possibility of injures when returning to Earth or stepping on the Martian surface.

Muscle atrophy is another problem that occurs due to weightlessness. It begins from decreasing the muscle volume. During a 6-month mission on the ISS the crew loss 10% to 16% in the calf muscles [20]. The volume change is inevitably leading to muscle strength, power and endurance. A decrease of 32 percent in peak muscle power (5.3% loss per month on average) has been observed in equal period aboard the ISS, despite the use of an exercise program incorporating treadmill running, cycling exercise, and resistance exercise [21]. HU induced on rats is showing that their muscle mass is decreased [22].

2. IMPACT OF THE IONIZING RADIATION

Earth's magnetic field is protecting us from HZE. However, in space flights not only HZE are danger to astronauts, but also galactic cosmic rays (GCR), solar wind, neutrons, electrons, mesons and γ-rays. It is not fully understood the action mechanism of IR to the biological tissue [23]. Some of the effects are leading to complex pathophysiological problems including single and double strand breaks in DNA [24], peroxidation of membrane lipids [25], formation of toxic products in free radical reactions etc.

Mars has a magnetosphere which in more than millionth time smaller than Earth's one [26]. This make Martian surface vulnerable to different types of radiation. For instance, GCR dose equivalent dose on the surface of 0.64 ± 0.12 mSv/day. An estimated a total dose equivalent of $\sim$1.01 Sv was calculated for a round trip mission to Mars, with a 180-daycruise, and 500 days on the Martian surface [27]. A possible prolonged mission into space could induce all above mentioned IR biological effects. But there are also changes in the neurochemical composition in the organism. Such experiment is done by V.S. Kokhan et al [28]. The authors' data shows the level of Serotonin (5-HT) is decreased by 20% in the IR group compared to the control animals and increased Acetylcholine (Ach) levels in the IR by 59%. This could lead to impairments in neuronal system and dysfunctions of other systems, depending of those mediators.

Another interesting result shows that the neuron length and area are decreased, when neuron cell cultures are irradiated with neutrons [29]. Also, there is accelerated apoptosis in the neurons due to high dose chronical radiation. However, small dose radiation has non-significant effect over the neuron integrity.

3. COMBINE EFFECTS

In space exploration, it is rare to observe only one factor. The two most common ones are microgravity and radiation. Despite this fact, there two opinions of their combine effect. First one is that weightlessness and IR are having synergetic effect. In combination of RPM and irradiation on neuron cell, Pani et.al [29] observed higher impact at apoptosis and morphology changes than observed alone. On the other hand, Kokhan et.al [28] are proposing that HU, as a microgravity model for rats, and radiation are acting like antagonists. The weightlessness has partly counteracted the negative effects of radiation.

4. SUMMARY

The scientific community has always come with different ideas in order to overcome any obstacles. Microgravity is one such. However, studies show that short term microgravity can enhance cognitive capacity or have slight change in the neuronal network [10, 11]. Other studies are suggesting that microgravity is having negative action on astronauts like inattention, difficulties in abstract thinking and task managing, neuronal network changes [13, 14, 29], skeletal system degradation [18, 19]. Few studies show different ways to counteract those effects. Xiang et al [30] suggest Repetitive transcranial magnetic stimulation for a possible method to overcome cognitive and synaptic plasticity impairment derived from weightlessness.

Drug administration can protect memory and cognitive deficit. The usage of ginseng is proposed for improving memory and cognitive impairments due microgravity [31]. Kai Xin San (KXS) is a traditional Chinese medicine which shows promising results in protecting and repairing cognitive deficit and oxidative stress. KXS is complex prescription comprising of ginseng, hoelen, polygala and andacorus [32].

To overcome the skeletal-muscle system deficit, National Aeronautics and Space Administration NASA) together with partner countries have developed various recommendations for the countermeasures, including procedures, training, exercise and counteracting drugs [33].

Despite the scientific breakthrough in the area of microgravity and ionizing radiation on the human body, a lot of research still have to be made in order to guarantee the astronauts mental and physical health.

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REFERENCES

[1] Christensen J and Talbot J. Review of physiological aspects of space sight. Aviation, Space and Environmental Medicine 1986; 57:203-212.

[2] Demontis GC, Germani MM, Caiani EG, Barravecchia I, Passino C and Angeloni D. Human pathophysiological adaptations to the space environment. Front Physiol 2017; 8:547

[3] Pietsch, J, Bauer, J, Egli, M., Infanger, M., Wise, P., Ulbrich, C., Grimm, D. The effects of weightlessness on the human organism and mammalian cells. Curr.Mol. Med. 2011; 11:350–364.

[4] Curtis SB, Vazquez ME, Wilson JW, Atwell W, Kim M, Capala J, Cosmic ray hit frequencies in critical sites in the central nervous system. Advances in Space Research 1998; 22:197–207.

[5] Morris R. Developments of a water-maze procedure for studying spatial learning in the rat. Journal of Neuroscience Methods 1984; 11:47-60

[6] Hall CS and Ballachey EL. A study of the rat's behavior in a field; a contribution to method in comparative psychology. Berkeley: Univ. of California Press 1932, Print

[7] Wassersug R, Izumi-Kurotani A. The behavioral reactions of a snake and a turtle to abrupt decreases in gravity. Zoolog Sci. 1993; 10:505-509

[8] Ronca AE, Moyer EL, Talyansky Y, Lowe M, Padmanabhan S, Choi S, Gong C, Cadena SM, Stodieck L, Globus RK. Behavior of mice aboard the International Space Station. Sci Rep. 2019; 9(1):10154

[9] Orr S, Weigand R, Adams T, Raychev R, Griko Y. Environmental Enrichment in the ISS Rodent Habitat Hardware System. International Journal of Bioscience and Medicine 2017; 1:6

[10] Wollseiffen P, Vogt T, Abeln V, Strüder HK, Askew CD, Schneider S. Neuro-cognitive performance is enhanced during short periods of microgravity. Physiology & Behavior 2016; 155:9-16

[11] Temple MD, Kosik KS, Steward O. Spatial learning and memory is preserved in rats after early development in a microgravity environment. Neurobiology of Learning and Memory 2002; 78(2):199–216

[12] Pani G, Samari N, Quintens R, de Saint-Georges L, Meloni M, Baatout S, Baatout S, Oostveldt PV, Benotmane MA. Morphological and Physiological Changes in Mature In Vitro Neuronal Networks towards Exposure to Short-, Middle- or Long-Term Simulated Microgravity. PLoS ONE 2013; 8(9): e73857
[13] Liao Y, Miao D, Huan Y, Yin H, Xi Y, Liu X. Altered regional homogeneity with short-term simulated microgravity and its relationship with changed performance in mental transformation. PLoS ONE 2013; 8(6): e64931
[14] Grabherr L, Mast FW. Effects of microgravity on cognition: the case of mental imagery. J. Vestibular Res. 2010; 20:53–60.
[15] Zhang Y, Wang Q, Chen H, Liu X, Ke Lv, Wang T, Wang Y, Ji G, Cao H, Kan G, Li Y, Qu L. Involvement of Cholinergic Dysfunction and Oxidative Damage in the Effects of Simulated Weightlessness on Learning and Memory in Rats. BioMed Research International 2018; Article ID 2547532
[16] Sun XQ, Xu ZP, Zhang S, Cao XS, Liu TS. Simulated weightlessness aggravates hypergravity-induced impairment of learning and memory and neuronal apoptosis in rats. Behavioural Brain Research 2009; 199(2):197–202
[17] Lang T, LeBlanc A, Evans H, Lu Y, Genant H, Yu A. Cortical and trabecular bone mineral loss from the spine and hip in long-duration spaceflight. J Bone Miner Res 2004; 19(6):1006-1012
[18] Keyak JH, Koyama AK, LeBlanc A, Lu Y, Lang TF. Reduction in proximal femoral strength due to long-duration spaceflight. Bone 2009;44(3):449-453.
[19] Baek K, Barlow AA, Allen MR, Bloomfield SA. Food restriction and simulated microgravity: effects on bone and serum leptin. J Appl Physiol 2008; 104:1086–1093
[20] Gopalakrishnan R, Genc KO, Rice AJ, Lee SMC, Evans HJ, Maender CC, Ilaslan H, Cavanagh PR. Muscle volume, strength, endurance, and exercise loads during 6-month missions in space. Aviat Space Environ Med. 2010;81(2):91-102
[21] Trappe S, Costill D, Gallagher P, Creer A, Peters JR, Evans H, Riley DA, Fitts RH. Exercise in space: human skeletal muscle after 6 months aboard the International Space Station. J Appl Physiol 1985;106(4):1159-1168
[22] Sculati M, Rossi F, Morlacchini M, Cena H, Roggi C. Diets with low glycemic index minimized weight loss in rats reared in a simulation of microgravity by hindlimb suspension. Nutrition Research 2007; 27:802–807
[23] Measurements, N.C.O.R.P.A. Radiation Protection Guidance for Activities in Low-earth Orbit: Recommendations of the National Council on Radiation Protection and Measurements. National Council on Radiation Protection and Measurements, Bethesda, MD., 2000
[24] Belov OV, Krasavin EA, Lyashko MS, Batmunkh M, Sweilam NH. A quantitative model of the major pathways for radiation-induced DNA double-strand break repair. J Theor Biol. 2015; 366:115-130
[25] Kiang, J.G., Fukumoto, R., Gorbunov, N.V., Lipid peroxidation after ionizing irradiation leads to apoptosis and autophagy. In: Catala, Angel (Ed.), Lipid Peroxidation. InTech, 2012
[26] Vaisberg OL, Ermakov VN, Shuvalov SD, Zelenyi LM, Halekas J, DiBraccio DA, McFadden J, Dubinin EM. The structure of Martian magnetosphere at the dayside terminator region as observed on MAVEN spacecraft. Journal of Geophysical Research: Space Physics 2018; 123:2679– 2695
[27] Hassler DM., Zeitlin C, MSL Science Team et al. Mars' surface radiation environment measured with the Mars science laboratory's curiosity rover. Science 2014; 343(6169): 1244797

[28] Kokhan VS, Matveeva MI, Bazyan AS, Kudrin VS, Mukhametov A, Shtemberg AS. Combined effects of antiorthostatic suspension and ionizing radiation on the behaviour and neurotransmitters changes in different brain structures of rats. Behavioural Brain Research 2017; 320:473-483
[29] Pani G, Verslegers M, Quintens R, Samari N, de Saint-Georges L, Oostveldt PV, Baatout S, Benotmane MA. Combined Exposure to Simulated Microgravity and Acute or Chronic Radiation Reduces Neuronal Network Integrity and Survival. PLOS ONE 2016; 11(5): e0155260
[30] Xiang S, Zhou Y, Fu J, Zhang T. rTMS pre-treatment effectively protects against cognitive and synaptic plasticity impairments induced by simulated microgravity in mice. Behavioural Brain Research 2019; 359:639-647
[31] Feng L, Yue X, Chen Y, Liu X, Wang L, Cao F, Wang Q, Liao Y, Pan R, Chang Q. LC/MS-based metabolomics strategy to assess the amelioration effects of ginseng total saponins on memory deficiency induced by simulated microgravity. Journal of Pharmaceutical and Biomedical Analysis 2016; 125:329-338
[32] Qiong W, Yong-Liang Z, Ying-Hui L, Shan-Guang C, Jiang-Hui G, Yi-Xi C, Jiang N. The memory enhancement effect of Kai Xin San on cognitive deficit induced by simulated weightlessness in rats. Journal of Ethnopharmacology 2016; 187:9-16
[33] Smith MA, Scholey AB. Nutritional influences on human neurocognitive functioning. Frontier in Human Neuroscience 2014; 8:358