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National Report on Space Medicine Progress

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Abstract The development of Chinese manned space engineering has a great role in promoting the progress of Chinese space medicine. With the accelerated implementation of Chinese Space Station Program, China's space medicine has made fruitful achievements over the past three years. This report summarizes the major progress of Chinese space medicine in terms of basic research and space applications from 2016 to 2018.

Key words Manned spaceflight, Space medicine, Countermeasures against weightlessness
Classified index V 7

1 Introduction

China's space medicine has made tremendous achievements with the initiation of the China Space Station Project (CSSP) and the successful completion of Shenzhou-11 and Tiangong-2 Space Laboratory mission since 2016. The issues related to the countermeasure against the physiological effects of weightlessness and the maintenance for astronaut's health have been basically solved. With the rapid advance of CSSP, the space experiment of human physiology and medicine which focuses on the key biomedical problems during long-term spaceflight, have been systematically planned and performed. Sustained and further development of basic research and application in space medicine have accumulated theories and technologies for the implementation of CSSP. Simultaneously, some active explorations and research, oriented towards a long-term plan of future deep space flight (*e.g.* manned Moon landing, Mars exploration), have also been carried out in the field of space medicine[1,2].

This report gives a brief introduction to the development of China's on-orbit and ground-based researches in space medicine and the related plans from 2016 to 2018.

2 Application and Research for Mid-term Flight

2.1 Astronaut's Health Maintenance

Duration of staying on orbit in Shenzhou-11 and Tiangong-2 mission has been extended to 30 days. The mid-term flight poses a great challenge to the health of the astronauts: changes in the cardiovascular system will experience the period of maximum response; muscle atrophy, bone loss and decline of the immune function will be more evident, and risk of disease increases. Furthermore, the 2-person crew is required to have higher emergency handling capability and psychological compatibility.

The crew members' physical and psychological conditions were kept well during the entire spaceflight mission, which was achieved by the comprehensive implementation of the countermeasures against the physiological effects of weightlessness, nutrition provision, psychological support, medical monitoring and support, and other related technologies. After returning, the crew members' routine physiological indicators recovered to their pre-flight levels within a relatively short duration.

Shenzhou-11 and Tiangong-2 mission enabled Chinese astronauts health maintaining technologies from a short-term to mid-term flights, and accumulated various space data on physical conditions, psychological state, energy intake amount, water intake volume, nutritional metabolism, and so on.

2.1.1 Countermeasures Against Physiological Effects of Weightlessness

Focusing on the major changes of physiology systems caused by mid-term spaceflight, including cardiovascular dysfunction, muscle atrophy, bone loss, immune function decrease, and so on, a countermeasure proto-

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col for physiological effects of weightlessness was studied and established, which accommodates the requirements for the 30-day stay of on-orbit astronauts, monitoring and evaluation of protective effects in astronaut against physiological effects of weightlessness.

2.1.2 Nutrition Provision and Supplementation

Based on the changes in the supply requirements of dietary nutrients, which is raised by prolonged spaceflight duration, the nutrient supply standards were studied and established with regard to reasonable energy absorption and supplementation against vitamins and minerals insufficiency. Vitamins and minerals were supplemented against the biomedical problems of bone calcium loss and insufficient vitamin intake during prolonged spaceflight. In addition, the variety of foods was enriched and the recipe and sensory acceptance were enriched, which improved the astronauts' appetite and. The on-orbit dynamic nutrition assessment and guidance were strengthened.

Nutritional provision and supplementation have solved the issues of dietary nutrient supply standards for mid-term spaceflight, further enriched the variety of foods, improved the acceptance of recipe and food sensory acceptance, and ensured the astronaut's on-orbit nutritional balance.

2.1.3 Psychological Support

For prolonged flight mission, the observation of psychological state was strengthened, and the medium and long-term flight psychological support model was explored, providing more comprehensive and effective psychological protection.

Psychological protection adopts a psychological support model that combines regular and on-demand measures, focusing on strengthening psychological state observation and psychological support such as psychological self-adjustment and targeted psychological intervention. Considering the individual needs and wishes of astronauts, more comprehensive and effective psychological support, based on the technology of bidirectional video and other technologies, were provided from both social and professional psychological support.

2.1.4 Medical Supervision and Security

The medical supervision and security have enhanced the detection and evaluation of cardiovascular function for mid-term flights. It has enriched the medical supervision indicators that have guiding value for the judgment of health status and disease diagnosis and added and verified medical monitoring techniques such as urinalysis and ultrasound.

The new telemedicine is a collaborative consultation, comprehensive use of the remote medical platform, database and other means to provide decision support for the medical treatment of complex medical problems. Neuromuscular stimulation is used for massage physiotherapy and auxiliary muscle function exercise.

2.2 Experiments On-orbit

China Astronaut Center (CAC) established Space Laboratory Project Team, which carried out studies on Human Health, Human Behavioral Research, Human Engineering Technology, and Human Safeguarding Technology Verification. There are 16 experimental studies and technical verifications in above 4 directions. Among them, 10 experiments in the field of space medicine on human health and human performance was completed.

2.2.1 Human Health Research

For 30 d flight in orbit, the cardiovascular physiology effect will begin to transit to the plateau after undergoing the peak change phase. "Cardiospace" cooperation between ACC and CNES was performed during Shenzhou-11 and Tiangong-2 mission to study cardiovascular function in space and to investigate the characteristics of the flight at different time intervals. This research is the first time in China to carry out on-orbit ultrasound testing, which verifies the interaction support mode of complex medical operation world and acquires valuable ultrasound imaging data of important organs. The cardiovascular and static physiological regulation characteristics of the cardiovascular system before and after the flight and different phases of flight were systematically acquired. The characteristic effects of space flight on the integrated physiological regulation mechanism of the cardiovascular system and the system were initially established. Integrating the cardiovascular physiological function analysis method laid the foundation for the mission-related technology application of the space station.

In other experiments, research data were continuously accumulated, such as aerospace nutrient metabolism, sleep-wake biological rhythms, on-orbit emotional characteristics, in-orbit noise effects, changes of smell in orbit, and pharmacokinetics.

2.2.2 Researches on Human Performance

In the space station, the mission on-orbit had become more difficult and more complex. Long-term flight and workload will affect the astronauts' mental load. The research on the change of on-orbit mental load can provide support for establishing techniques of brain load assessment during long-term flight. At the same time, it continuously collects astronaut on-orbit coordination data.

3 "Space 180" Experiments

The 4-person 180-day integrated experiment in CELSS was aimed to develop biological regenerative life support and health maintenance technologies on future engineering applications. It was designed and operated for a monthly/firebase controlled ecological life support system, with long-term closure, a high degree of material closure, and characteristic integrated ecological healthcare system integration technology. With the characteristics of biology regeneration, organic integration of physical-chemical regeneration and environmental control technology, a third generation environment control and life support system suitable for multi-occupant was constructed[3].

The 4-person 180-day integrated experiment achieved more than 1700 data collections between the controlled ecological life support technology and medical experiment research, which accumulating valuable experience in expanding the scientific exploration of human living space. Among them, human-environment interaction research mainly focuses on the following five aspects: psycho-physiological interaction research, biological rhythm research, molecular methylation, health intervention and human factor and sound environment evaluation. There were 15 medical experiment projects including teams from France and Germany.

4 Researches on Ground-based Experiments

Focused on microgravity physiological effects, space radiation, environmental factors, space human behavior and cognitive effects, space nutrition, drugs for protection, and related technologies for space medicine experiments, researches were carried out on ground-based experiments from molecules, cells, organs, and the body level, to explore the effects of mid & long-term spaceflight on astronauts and health maintenance measures.

4.1 Microgravity Physiological Effects and Coutermeasures

4.1.1 45 d-6° Head-Down Bed Rest (HDBR)

45 d-6° HDBR caused a significant decrease in physical exercise cardiopulmonary function. Traditional Chinese medicine Hongyi capsule can effectively counter this type of decrease[4]. The moderate-intensity exercise based on artificial gravity can effectively resist the decrease of endurance and anaerobic exercise tolerance caused by 45 d-6° HDBR[5].

4.1.2 Researches on Muscle Atrophy

Researches on miR-491 identified it as a novel negative regulator of myogenic differentiation through targeting myomaker[6]. Studies on Bu Zhong Yi Qi decoction (BZ) indicated that BZ could protect muscles from simulated weightlessness induced atrophy. BZ significantly downregulated nuclear receptor corepressor 1 (NCoR1) expression, and further induced muscle differentiation and metabolism by regulating NCoR1associated gene expression in vivo and in vitro[7]. The study of plasticity and mechanism of muscle satellite cells in weightless muscle atrophy revealed that in the process of weightless muscle atrophy, the number of muscle satellite cells in silence was significantly increased, and the number of activated satellite cells was significantly decreased, and the muscle satellites with myogenic differentiation potential were observed. By comparative analysis of the Smad3 gene knockout and its littermate wild-type mice, the differences in the plasticity of muscle satellite cells in weightless muscle atrophy revealed the key role of Smad3 in regulating the plasticity of weight loss muscle atrophy satellite cells[8].

Results of multi-electroacupuncture stimulation on the soleus muscle atrophy in simulated weightless rats showed that the number of nuclei increased and no inflammatory cell infiltration was observed in the 30 d tail suspension and multi-acupoint stimulation group compared with the 30 d tail suspension group[9].

4.1.3 Researches on Drugs

Studies showed that crushed bone debris can promote bone cell proliferation under weightlessness, and its mechanism is related to the activation of the ERK pathway[10]. Other researchers observed the effects of total flavones of rhizoma drynariae on the proliferation of osteoblasts and JNK pathway changes under weightlessness. It was concluded that rhizoma drynariae can promote the proliferation of osteoblasts under simulated weightlessness, its mechanism may be achieved by inhibition of the JNK pathway[11−13].

Effects of natural product functional components and calcium ion-bound chelates on mice by tail suspension to simulated weightless was explored, and results showed that the black fungus peptide calcium chelate has a certain degree of protective effect on bone loss in the mouse by hindlimb unloading model[14]. Effects of astragaloside A and vitamin D3 on the proliferation of primary rat osteoblasts in two-dimensional rotational cultures: a single use of astragaloside or vitramin D3 both promotes the proliferation of normally cultured osteoblasts and promotes proliferation[15]. Under simulated weightlessness, different doses of EPCP showed different protective effects on osteoblast cycle, apoptosis, and alkaline phosphatase activity, respectively[16].

It showed that acanthopanax senticosus saponins could improve the blood fat, blood glucose and immune function of rats induced by simulated weightlessness for 4 weeks, and had little effect on liver and kidney function[17]. The efficacy of levofloxacin in the treatment of infectious pneumonia is reduced under the simulated weightless environment[18].

4.2 Environmental Medicine

4.2.1 Space Radiation Effects and Protection

Research on space radiation impact and protection focuses on solving the effects of space radiation risk factors, studying the biological hazards of aerospace special environmental factors on the organism and its mechanisms, and putting forward effective protective measures. Studies using juvenile squid as an experimental animal have found that mimicking spatial radiation on the ground can cause adverse effects such as oxidative stress, metabolic disorders, the death of cell programming, and fluctuations in DNA damage and oxidative phosphorylation[19].

4.2.2 Noise Studies

The impact of in-cabin environmental factors and protection research focuses on solving the effects of harmful factors such as noise in manned spacecraft, studying the biological hazards of the cabin environment and its mechanisms, and putting forward effective protective measures. A recent study shows that the level of mental workload of the participants in the implementation of the same working memory task in a noisy environment can be increased, but the improvement is reduced when the task is difficult[20].

4.3 Cognitive and Behavior

Effect of changes in posture for 30 minutes on intraocular pressure and visual acuity was studied and the results revealed that under the effect of microgravity, the intraocular pressure will increase and the overall visual ability will probably decrease[21].

Simulated weightlessness in tail suspension can affect the morphology and number of hippocampal neurons in rats, down-regulate the expression of learning and memory-related molecules, and up-regulate the expression of proapoptotic-related molecules[22].

The research on the application of voice interaction technology in the remote operation of the robot arm shows that, for the semi-autonomous control task of the robot arm, the voice control method can obviously improve the operation speed, reduce the control difficulty, reduce operating load, visual and cognitive load processing load[23].

4.4 Space Nutrition

Observed effects of hydrogen-rich water on rats' intestinal microflora under simulated weightlessness showed that the copy number of enterococci and E. coli in the intestine increased, while the copy number of C. perfringens decreased, and hydrogen-rich water on the intestine Cocci have a significant inhibitory effect[24]. 30-day HDBR can cause a significant decrease in the number of bifidobacteria, which suggests that the simulated weightlessness leads to intestinal flora imbalance, edible composite living bacterium preparation can be in a certain extent, promote the proliferation of bifidobacteria, can antagonize the intestinal flora disorder by simulated weightlessness[25].

4.5 Advanced Researches

4.5.1 Technologies for Space Medical Experiments

Space medicine research needs the support of special experimental equipment that adapts to the aerospace environment. The development of technologies for on-orbit of cells and overall medical experiments can provide important support and guarantees for space medicine research. Such R&D have made progress rapidly, for example, a controllable internal flow path, with anti-leakage, anti-pollution ability of the entire transparent and closed cell culture plate[26], and a kind of reliable performance, simple operation and maintenance, low cost and bring valve control function of the pump head split type dc micro motor driven peristaltic pump[27] was developed recently.

4.5.2 Studies for Lunar Mission

Simulating the effect of lunar gravity on the human cardiovascular system and its autonomic regulation characteristics showed that compared with the supine position, the control group had a higher heart rate and a higher diastolic pressure during the period of bed height of 10°. There was no significant change in heart rate and blood pressure in the socks group. It shows that there is no obvious change in heart rate and blood pressure under simulated lunar gravity conditions, but the autonomic control is increased.

Lower limbs wearing a compression sock combined with a bed height of 10° can be used to simulate the effects of lunar gravity on human cardiovascular[28].

A study using Lunar Soil Simulant (LSS) to explore the pathological changes of acute lung injury induced by LSS was completed. It indicated that LSS may have stronger pulmonary toxicity than PM2.5, which can cause lung parenchyma damage and produce inflammatory lesions[29].

The study of space radiation risk assessment conducted by a simulated manned lunar exploration mission showed that as the shielding thickness increases, the astronaut's absorbed dose and dose equivalents and effective doses of various tissues or organs are significantly reduced. The method of mass screening has a good protective effect on protons below 100 MeV, but the protective effect on high-energy protons or heavy ions is not obvious. The calculation and analysis show that the space radiation risk of the astronauts is controllable as long as appropriate protective measures are taken during manned lunar exploration[30].

5 Future Expectations

More than 50 years of manned space flight shows that deepening the understanding of the physiological effects under microgravity and advance the protection capability is the primary task for space medicine.

The systemic regulation theory that forms the physiological effects of weightlessness and its mechanisms is an important direction for the study of physiological mechanisms of weightlessness. In the future we should focus on the efficacy of weightlessness against protection, in-depth study of the dose-effect relationship and individualized solutions of power load and endurance load, and develop the follow-up, target, and intelligent integrated protection technology based on Chinese traditional medical theory and latest knowledge discovery. It is highly concerned about the ability of gravity re-adaptation after the long-term flight, and the active recovery technology after development. To expand the application of health risk assessment, early warning, and management based on data platform construction. At the same time, space station medical applications should be taken as the traction, facing the goal of surviving from the ground, and promoting the construction of major national scientific research infrastructure based on simulated low-gravity and artificial gravity integrated system platforms and theoretical and technical reserves for follow-up missions.

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