ISSN 0233-528X

Aerospace and Environmental Medicine

АВИАКОСМИЧЕСКАЯ И ЭКОЛОГИЧЕСКАЯ МЕДИЦИНА

From Gagarin's first Orbit to international Space Journey

XXIII INTERNATIONAL SYMPOSIUM

HUMAN IN SPACE

1961 2021

April 5–9, 2021

Moscow, Russia

2021 V. 55 № 1/1 special issue

The Organizers:

INTERNATIONAL ACADEMY OF ASTRONAUTICS (IAA)

STATE SPACE CORPORATION "ROSCOSMOS"

MINISTRY OF SCIENCE AND HIGHER EDUCATION
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Aerospace and Environmental Medicine
AVIAKOSMICHESKAYA I EKOLOGICHESKAYA MEDITSINA

SCIENTIFIC JOURNAL

2021 V. 55 № 1/1 special issue

Founded in 1967

1967 – 1974 – «Space Biology and Medicine»
1974 – 1991 – «Space Biology and Aerospace Medicine»
1991 – «Aerospace and Environmental Medicine»

INCLUDED IN THE LIST OF THE LEADING REVIEWED JOURNALS HIGHER ATTESTATION COMMISSION OF THE RUSSIAN FEDERATION

Founder and publisher

The Russian Federation State Research Center – Institute of Biomedical Problems of the Russian Academy of Sciences (IBMP RAS)

The journal is registered by the State Committee of the Russian Federation for Press 28.02.1995, reg. № 01072, license ID number 05859 on 18.09.2001

Managing Editor, technical editor and proofreader – Sorokin O.G., Ph.D.
DTP – Rzaeva E.V.

Address: 76A, Khoroshevskoe shosse, Moscow 123007, Russia
Institute of Biomedical Problems of the Russian Academy of Sciences (IBMP RAS)
Journal of Aerospace and Environmental Medicine. E-mail: arhiv@mail.ru, tel. 8 (499) 195-65-12
Fax: 8 (499) 195-22-53
Publishing office
E-mail: library@imbp.ru, tel. 8 (499) 195-68-74

Сдано в набор 26.02.2021
Подписано в печать 09.02.2021
Формат 60 × 84 1/8
Гарнитура Tahoma
Печать офсетная
Усл. печ. л. 17,7
Тираж 300 экз
Заказ № 35

Отпечатано в типографии ООО ИПЦ «Научная книга»
Адрес: 394026, г. Воронеж, Московский пр-т, д. 116

INTERNATIONAL ACADEMY OF ASTRONAUTICS (IAA)
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Abstracts

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NASA ARTEMIS MISSIONS & HUMAN RESEARCH OPPORTUNITIES

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NASA's Artemis program will return humans to the Moon and establish sustainable exploration, to help prepare humanity for the next giant leap to Mars. Artemis missions offer platforms to study human health and performance in the deep space environment, and the Human Research Program (HRP) is actively working across Artemis programs and with international partners to enable human research opportunities.

This is an exciting opportunity to collect invaluable human health data to expand our understanding on the influence of various spaceflight hazards on humans with the goal of Mars exploration-class missions. Artemis platforms for potential utilization include in-flight Gateway, lunar surface science, pre-deployed payloads, pre- and post-flight baseline data collection, and transit in the Orion vehicle between Earth and lunar vicinity.

This session will include an overview of Artemis missions and their components, general mission timeline, plans for Initial Capabilities, including human research opportunities, and an overview of Sustained Capabilities and Mars-forward missions. Additionally, it will describe the need to synergize human research and medical operations for Artemis missions with their limited mission opportunities and constraints.

NEUROPSYCHOLOGICAL EFFECTS OF ISOLATION AND PHYSICAL EXERCISE REGIMEN DURING SIRIUS-19

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Physical exercise could reduce the risk of undesired mental impairments during isolation and space missions. This project aimed to clarify beneficial as well as adverse effects of continuous versus interval running exercise on brain health and cognition and underlying neurophysiological mechanisms during a terrestrial simulated space mission.

Six volunteers (aged 33.6 years, 3 females) simulated a 120-day mission to the Moon (SIRIUS-19). Exercise training consisted of treadmill running during a continuous (CON) or an interval (INT) protocol. Each protocol was performed throughout one half (either first or second) of the mission and switched in a cross-over design. Data was collected prior to (BDC-14 to BDC-7), four times during (start and end of each protocol; MD14/16, MD53/54, MD79/80, MD110/112), as well as post isolation (R+6 to R+9), pre- and post- exercise on two separate days respectively. Cognitive performance (Cognition test battery BHP-SM), self-perceived state of mood (MoodMeter©) and affect (PANAS), and electroencephalographic recordings (EEG, 32-channel) were assessed. Morning blood samples were drawn to assess BDNF, IGF-1, and VEGF and saliva samples every 2 hours from 8am to 10pm to assess cortisol levels. Effects of isolation (factor: TIME), exercise (pre vs post exercise), exercise protocol (INT vs CON) and gender were calculated using non-parametric tests. No significant changes from in to post isolation data collections have been observed. Therefore, only BDC was compared to the end of each training protocol in order to reduce alpha error and increase statistical power ($\alpha = 0.05$, for factor time $\alpha = 0.017$). As an effect of TIME, lactate decreased at fixed running speed 9km/h ($p = 0.03$) at the end of both training protocols compared to BDC ($p = 0.046$). Cortisol level increased as a factor of time ($p = 0.011$) from BDC to the end of both exercise protocols ($p = 0.028$) and cognitive performance improved (overall reaction time $p = 0.006$, score $p= 0.016$). Positive ($p = 0.549$) and negative affect ($p= 0.717$) as well as perceived physical ($p= 0.568$) and motivational state ($p= 0.200$) did not change over time. Perceived psychological strain significantly improved comparing BDC to both exercise protocol end-points ($p = 0.015$). Neither BDNF ($p = 0.607$), IGF-1 ($p = 0.60$) nor VEGF ($p = 0.846$) did change over time, but IGF-1 showed a significant effect of exercise protocol and higher values at the end of CON compared to the end of the INT protocol ($p = 0.028$). With this exception, no difference between pre and post exercise, exercise protocols and sex were found for all other variables. Reduced broadband power and a flattening of the 1/f spectral slope was found in resting-state EEG during isolation compared to BDC (see Weber et al. Scientific reports (2020)10: 17987).

In conclusion, this exercise training protocol during 120 days of isolation improved physical fitness. Although cortisol level increased and brain cortical activity decreased during isolation, cognitive performance, mood, affect and neurotrophic factors remained stable independent of gender and the exercise protocol (except IGF-1 increased for CON). Longer duration missions with manipulations of the exercise protocol are needed to further optimize training protocols.

HUMAN SPACEFLIGHT OUTREACH – CHALLENGES AND STRATEGY FOR A DEVELOPING NATION

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As humanity celebrates the 60th anniversary of the first human spaceflight endeavor, human spaceflight activities are evincing greater interest from around the globe. This is truly democratization phase of human space activities as more nations are beginning to understand the benefits of a sus-tained human spaceflight program. Human space programs pursued by nations have undergone a transformational shift from being a tool of projection of national power and technological prowess to symbols of international cooperation. Today, these programs are transcending national borders as the benefits of scientific research and spin offs, are percolating to the common masses. Yet the classic argument on the benefits of human spaceflight vis-a-vis its economic costs still constrain many poli-cymakers to take bold national initiatives in this area. This is especially true in the case of developing nations where public resources are scarce.

Space education and outreach activities provide an effective tool to address this issue as an ena-bler for mass participation in human space activities. This is evident from the fact that space travelers have been regarded as role models to society and ambassadors of humanity beyond their national borders. There is a need to utilize space education and outreach tools innovatively for information dissemination, taking into account the information needs of all the stakeholders. This improves trans-parency about the program goals and outcomes.

In the case of human spaceflight activities in developing nations, this becomes especially im-portant as public enthusiasm, participation, and support of human spaceflight activities is an im-portant investment driver. Effective outreach program also facilitates international cooperation. In addition to this, space education and outreach also help in the development of scientific tempera-ment and curiosity among the masses, especially youth. This is the main driver for technological in-novations, entrepreneurship, and spurring business growth, which is essential for the economic de-velopment of any nation.

This paper discusses the contribution of space education and outreach activities in the domain of human spaceflight and its socio-economic impact. This paper also addresses the challenges in space education and outreach activities that are unique to developing nations and proposes strategies to overcome. This paper also argues that Space agencies especially from the developing world who as-pire to pursue human space activities must implement a comprehensive Space education and out-reach strategy.

GOVERNANCE OF SPACE TOURISM

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Tourism has been a key driver for socio-economic development in many countries around the world. In the year 2019, global travel and tourism activities contributed around 10 % to the world's GDP and 1 in 10 jobs around the world was generated by tourism industry. This is a consumer driven industry where the demand is met by various service providers and competition drives the quality of services.

Space travel and tourism holds a promising future as an economic activity and adds another di-mension to the present travel and tourism activity on earth. This paper aims to present a model for the space travel and tourism industry and analyses the role of different stakeholders. Space activities have played a major role in the development of humanity through the planetary exploration; micro-gravity based scientific research and spin-offs. Space travel has been the domain of governmental space agencies in space faring nations. However, with the entry of private players in space activities, space tourism may become a reality in near future.

Compared to the travel and tourism activities on earth, space travel and tourism has additional dimensions and therefore stakeholders. This paper proposes a governance model involving different stakeholders in space tourism sector. This is done while factoring in various consumer profiles and the demand scenarios. Since space travel is inherently a hazardous activity, role and jurisdiction of regulatory agencies is also discussed.

SOLVING NUTRITION PROBLEMS IN INTERPLANETARY SPACE FLIGHTS

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The solution of issues on the development of products and food rations that ensure the preservation of the health and performance of crews when exposed to the body of adverse environmental factors during flights into deep space is one of the main areas of work in the creation of food supply systems (SOP) for crews of interplanetary manned transport ships.

When developing SOPs for interplanetary flights, the principle of continuity should be observed, when the design and layout of a new system uses well-proven and improved SOP elements of previous manned transport ships and orbital stations.

The conditions of interplanetary flights determine a number of additional problems that need to be solved in the process of creating an SOP. These include, first of all, long flight autonomy and high levels of ionizing radiation when passing through radiation belts.

The lack of the possibility of periodic replenishment of stocks during interplanetary space flight is associated with special requirements for food rations in general and for their constituent products. The main of these requirements are:

- minimum dimensions and weight; - ease of use and storage in a spacecraft;
- convenience of food intake and its "unfeasibility" for a long time;
- minimal time spent on cooking and the possibility of using them both hot and cold;
- good digestibility and assimilation;
- microbiological safety during the entire storage period.

To ensure the safety of crews during the passage of radiation belts, it is necessary to develop and introduce into the diet products with radioprotective properties and biologically active products, which will significantly expand the arsenal of means for protecting the body from ionizing radiation and preventing functional changes developing in the body when exposed to extreme factors during flights into deep space.

In addition to the main diet on board the interplanetary spacecraft, a wide range of additional food sets and special food and food additives should be available. They will make it possible to introduce variety in nutrition, to correct the nutritional composition of rations in accordance with the changing needs of the body at various stages of a space expedition, to ensure the normal functioning of the gastrointestinal tract, excretory system and other physiological processes in the body.

Conclusion. In order to provide physiologically adequate nutrition for spacecraft crews during flights into deep space, it is necessary to start developing:

- Technical equipment for modernization of the SOP on an interplanetary manned spacecraft;
- Technologies for the manufacture of a new range of products for long-term (at least 3 years) storage;
- Products with radioprotective properties and biologically active products that increase the body's resistance to adverse environmental influences and reduce the risks of developing certain diseases.

APPROACH FOR EVOLVING MEDICAL CRITERIONS & HUMAN TOLERANCE LIMITS FOR FUTURE SPACE TOURISTS

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As Space Tourism is an upcoming lucrative sector with immense commercial potential. With the ad-vent of private players in commercial human space sector the space tourism sector is only expected to grow further. Unlike the Space Mission in pursuance of scientific objectives, a commercial tourist flight is likely to change the philosophy of designing a Space Mission significantly.

Designing a space mission is a challenging task which in turn strives to strike a balance technical limitations in terms of the capability of rocket system, weight of crew module, operational requirement for safe recovery at all stages of launch and recovery and need to keep various physical stressors like acceleration, vibration, noise and temperature etc. within the tolerance range of the subjects occupying the crew module.

Commercial spaceflight missions are bound to adopt crew safety measures which include continu-ous abort capabilities. Thus for a commercial tourist spaceflight another challenges that designer shall address is human tolerance limits to be defined in case of mission aborts.

Currently the standards available on human tolerance limits are applicable to selected group of ex-tremely healthy and well-trained Astronauts/ Cosmonauts. Space Tourism will result in demands similar to present day aviation industry. It is expected that people from all walks of life with wide variation in physical attributes and health status will be the target consumer.

The future space tourist may not ideally possess optimum health status as per current standard. Al-so for a space tourist the expected tolerance level, to the physical stressors encountered during the space mission is expected to be less.

This paper deliberates upon various aeromedical and engineering challenges in designing a 'safe and pleasant' space mission profile for future Space Tourists. The authors through this study have at-tempted to evolve medical criterions, tolerance limits, and mission specifications suiting the target pool of space tourists.

APPLICATION OF A NEURAL NETWORK IN A MOBILE DEVICE TO MONITOR THE STATE OF AN ASTRONAUT'S HEART DURING A FLIGHT

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The development of tools and systems for monitoring the health of specialists in space expeditions has many reasons. The work of an astronaut requires certain guarantees of timely detection of deterioration in the health and performance of a specialist, and in some cases - his falling asleep due to accumulated fatigue. In space flights, the working environment is aggravated by weightlessness, artificial gravity, radiation background, cramped space, constant crew environment, space suit limitations, and fears of possible failure of the station nodes. Carrying out external, repair work, landing on the surface of a new planet a priori should rely on medical sensors placed on the body or inside the spacesuit.

Performance of load tests and training, even taking into account the safe operation of on-board systems, is also more convenient to perform with the use of portable devices that have intelligence. However, wearable diagnostic technology is still developing. Holter heart monitors only store data in memory and require a medical analysis of the ECG.

The aim of the study is to increase the functionality and mobility of astronaut heart monitoring devices by using artificial neural networks in the analysis of electrocardiosignals (ECS).

The authors propose their own portable cardioanalyzer with neural network processing, which provides reliable information about the state of the heart in conditions of free activity. When forming a diagnostic conclusion about the state of the astronaut's heart, its localization, stage of development (peracute, acute, subacute or scarring) and the type of lesion depth are indicated. For this purpose, neural network analysis of the state of the heart is used, which consists in registering a continuous electrocardiosignal (ECS) (in L leads), pre-processing and presenting it as an n-dimensional vector (for L leads), creating model n-dimensional vectors of various ECS (for L leads), training neural networks, performing neural network analysis of n-dimensional ECS vectors, analyzing the outputs of neural networks based on the construction of decision rules, and displaying the result about the state of the astronaut's heart.

Conclusion. Analyzing popular gadgets and mobile applications, it should be noted that their functions do not meet flight requirements and are designed only to stimulate physical activity. The development of wearable smart devices that report depletion of body resources can help solve the problem of independent control of vital functions in astronauts

CEREBRAL ACTIVATION TO IMAGINATION OF SPATIAL NAVIGATION IS ALTERED AFTER 6 MONTHS IN MICROGRAVITY

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Introduction. Cerebral plasticity induced by prolonged exposure to (simulated) microgravity has been observed in structural as well as passive stimulation and even resting state MRI. In space, the representation of and interaction with the environment is altered due to microgravity in numerous ways including the ability to orient through a 3D space and adapted muscle control. In the current study, we aim to investigate how cerebral activity is altered after spaceflight when performing spatial navigation and motor imagery tasks.

Methods. Functional MRI of 12 Russian Roscosmos cosmonauts were acquired approximately 3 months pre launch to the ISS (± 6 months) and approximately one week post return to Earth. Eight of the subjects were also scanned at follow-up (>6 months <1 year later). Age and gender matched healthy controls (HC) were scanned at similar intervals as the pre- and post scan of cosmonauts. Participants were instructed to mentally navigate through a familiar place and instructed to imagine playing tennis to induce activity in cerebral motor systems. fMRI data was acquired (TE/TR=30/2000ms, $3mm^3$ voxel, full brain field of view) with eyes closed while performing a mental imagery task (15 scans) and resting state (15 scans) in a block design for 165 scans (±5.5 min).

Data was motion corrected, coregistered to the structural image, segmented, normalized and smoothed using a smoothing kernel. A GLM analysis was performed in SPM12 to measure task activation (1^{st} level analysis) and contrasting this (separately for the two tasks) with activation during rest over the different timepoints (2^{nd} level analysis), within the cosmonaut and HC groups. Third level analysis was performed to investigate group differences in the changes over the time points. Results are considered significant at 0.001 uncorrected (2^{nd} level analysis) or cFWE 0.05 (3^{rd} level analysis).

Results. Cosmonauts performing the spatial navigation task after return to earth have a decreased activation of the supplementary motor area, midfrontal cortex, Operculum, insula, putamen and cerebellum (uncorrected) as compared to preflight. Cosmonauts compared to healthy controls show decreased activation in the insula, superior temporal gyrus and putamen for the pre- compared to post- scans (cFWE $p < 0.05$). Pre- and post- measurements do not differ from follow-up flights. Activation during the tennis task was not affected by microgravity for either timepoint and neither in comparison with healthy control subjects. The healthy controls did not show any difference in activation for either timepoint or task.

Discussion and conclusion. Cosmonauts show reduced activity post-flight in the navigation task, and not for the tennis task. This suggests that altered orientation cues for about 6 months alters cerebral networks involved in navigation. These results seem to be in line with the observation that functional connectivity changes affecting similar regions during plantar stimulation (creating the suggestion of walking) during fMRI. At follow-up the activation seems to be normalized to pre-flight values which indicates the temporary nature of our finding, although incomplete follow-up data might bias our results.

PSYCHOLOGICAL AND PSYCHOPHYSIOLOGICAL CHRONIC STRESS PREDICTORS

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Relevance. Solving problems related to the assessment and forecasting of development chronic stress (CS) remains a relevant area of work on psychological ensuring the professional activities of specialists in hazardous professions with making responsible decisions, operators, whose mistakes can lead to serious social and economic consequences. It is due to the presence in them activities high emotional and neuropsychic pressure, as usually leading to the development of chronic stress, which increases the risk of occurrence, for instance, piloting errors, aviation accidents, professionally significant diseases and a reduction in occupational longevity. Use for these purposes psychodiagnostic techniques have shown their effectiveness. However, the data of psychologists onsusceptibility of some of them to motivational distortions, lack of validity and predictability necessitates research in order to isolatethe necessary and sufficient number of indicators that can be defined as CS predictors.

Target. Based on a comprehensive study of the informative value of indicators psychological and psychophysiological techniques used in the course psychological support for the professional activities of hazardous professions, to highlight the indicators of methods that increase the objectivity of assessment andpredicting the development of CS.

Material and methods. The results of psychological (including psychophysiological) examination were subjected to a comprehensive analysis using techniques thatallow, according to the authors and researchers, determining the level of neuropsychic, psychoemotional stress (diagnostics of the motivational structure of the personality (Milman), Rasskazov, Gordeeva and Osin methodology of adaptation, the Spielberger-Khanin method for identifying personal and situational anxiety, etc.). The presence of statistical links between diagnostic indicators and the presence of CS symptoms, health disorders was studied. A method was developed for integrating the results of psychological examination in order to obtain decisive rules for assessing and predicting the development of CS.

Discussion. Literature soursesresearch and statistical analysis allowed us to select indicators that corresponded to those formulated by us the principles of selection: the presence of confirmed links between assessments and manifestations of chronic stress, the adequacy of the use of method scales according to their belonging to the normal distribution, as well as the methods used by the authors for the integration of psychodiagnostic assessments. The identified indicators reflect the operator's motivational profile, strategies for the response style in dangerous conditions, the severity of chronic fatigue and the degree of personal anxiety, adaptive potential and the level of professional burnout. To be used by psychologists, the list included techniques whose indicators had high coefficients of importance.

Conclusion. The study made it possible to clarify the list of psychological and psychophysiological methods, the indicators of which can be considered as CS predictorsin operators, which increases the objectivity of its assessment and development forecasting.

RAT BONE TISSUE IN CONDITIONS OF LIMITED MOTOR ACTIVITY

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It's believed that there are two main sources of regulators of mechanical transduction of bone tissue - exogenous gravitational forces and endogenous muscle forces. But, there is no convincing evidence for a leading role in the regulation of bone metabolism of muscle strength. This fact determines the novelty of the proposed study. The aim of the work is to assess changes in the mechanical properties of rat bones with a decrease in the physical component of movements and a decrease in their total number (hypokinesia), and in the other case - the tonic component and muscle load, support (hypodynamia).

Restriction of the motor activity of rats was achieved by placing them in pencil cases. By moving the partition, the volume of the box was changed according to the size of the animal. The hanging method according to Morey-Holton modified by Ilyin and Novikov was used as a model of gravity unloading. All experiments were performed in compliance with bioethical standards.

The bones were weighed, the density was estimated, the geometric parameters were measured, and then the three-point bending tests were carried out.

The results showed that in the case of antiorthostatic suspension and hypokinesia, unidirectional changes occur – loss of strength and stiffness of the femur and humerus and an increase in the ulna and tibia in adult animals. It was also shown that the femurs lost bone mass faster than the lower legs. For the young rats, it was shown that a loss of both strength and stiffness of the bone, also more pronounced in the femur and humerus. The data show that the mechanical properties of bone decrease significantly under hypokinesia.

This work was supported by the Russian Science Foundation (RSF grant No. 18-75-10027).

MODELING OF BONE ORGANS UNDER THE INFLUENCE OF EXTERNAL FORCE FACTORS

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It is known that bone formation is defined by exogenous gravitational forces and endogenous muscle forces. On another way, the question of the quantity of influence of each factor on bone remodeling is still ongoing. Wherein, the mathematical formulation of Wolf's law is known. The aim of the work is to evaluate in numerical experiments the influence of various force factors on the formation of a bone tissue organ.

The femur was used as a model. The initial geometry was modeled by two cylinders smoothed by spheres, with an evenly distributed material. For the resulting geometry, geometric and anatomical parameters were introduced. Three problems were formulated: pure impact of mass forces, the impact of support forces, and impact of muscle forces. The solution was produced numerically based on the finite element method and projection methods. The general numerical model was subjected to nondimensionalization.

As a result of modeling, a clear shaping of the femur was revealed: the formation of the tubular component of the long bone, strengthening of the material in the area of the Adams arch, the formation of the greater and lesser trochanters. As a result of modeling, the characteristic forms of the femur were revealed depending on the external influence.

This work was supported by the Russian Science Foundation (RSF grant No. 18-75-10027).

FEASIBILITY STUDY OF HABITAT DESIGN COMMONALITIES FOR MARS TRANSIT AND SURFACE MISSIONS

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This paper discusses the feasibility of developing a Mars surface habitat with capabilities that present certain commonality with in-space transit habitat architectures. The presented study follows mission requirements that are defined in NASA's

Human Exploration of Mars Design Reference Architecture 5.0. The applied methodology includes the analysis of reference mission requirements, examination of functionality and constraints for surface and in-flight conditions, definition of principal characteristics of the habitat that are specific to each environment, and summarizing those characteristics to develop design evaluation and selection criteria.

The long term vision for this feasibility study is the development of habitat architecture that can be effectively adjusted and scaled for multiple mission needs while providing livable and comfortable environment for the crew. Creating habitable environments with common capabilities for habitation in-space flight conditions and the Mars surface environment relies on substantial progress in most technology areas defined in NASA's Evolvable Mars Campaign. This paper discusses the possibility for designing a common module layout for zero- and partial gravity conditions. Furthermore, the paper presents design considerations for addressing commonalities, based on the analysis of mission goals and objectives, human factors considerations and challenges of design implementation.

MORPHOLOGICAL CHARACTERISTICS OF BLOOD VESSELS AND CYTOKINE REGULATION OF COMPENSATORY REACTIONS IN THE RESPIRATORY ORGANS OF RATS UNDER THE EXPERIMENTAL FLUID SHIFT IN THE CRANIAL DIRECTION

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The cytokine activity of local homeostasis in the lung tissue, the morphology of compensatory reactions in blood vessels, the changes in the epithelial structures of the trachea and lungs in animals when modeling of the fluid shift in the cranial direction (antiorthostatic suspension) have been studied.

Experimental studies have been carried out on male Wistar rats weighing 180–200 g. Antiorthostatic hanging was carried out for 15 days according to Novikov-Ilyin method with Morey-Holton modification.

Cytokine regulation of intercellular interactions was assessed by IL-10, IL-4, TNFa, TGFb1 in the lung tissue homogenate using enzyme-linked immunosorbent assay (ELISA).

The morphology in mucous membrane of the trachea and respiratory part of the lungs was characterized by the dilatation of the venous vessels, looseness of connective tissue, diapedesis of leukocyte cells through the vascular wall, and spasm of the arteries.

Apparently, stagnation of blood in the vessels of the lungs is accompanied by an increase in their permeability, which leads to the appearance of serous fluid and blood cells in the lumen of the airways and can provoke the development of inflammatory reactions.

However, no significant changes in the activity of pro- and anti-inflammatory cytokines (IL-10, IL-4, TNFa, TGFb1) were observed during this period, which indicates the absence of pronounced structural and functional disorders in the respiratory organs, requiring active cytokine regulation of the immune response.

On the 90th day of the recovery period, there are no signs of venous stasis in the tracheal wall and in the lungs. In the trachea, lymphoid cells are preserved only in the submucosa. The epithelial layer has a normal structure: there is a decrease in the number of goblet cells and an increase in the number of ciliated cells and a thickening of the brush border. In the basal layer, cambial cells are actively proliferating.

In the respiratory part of the lungs, in some areas, the alveolar walls are thickened due to the proliferation of pneumocytes. There are fibroblasts and thin collagen fibers between the walls of the alveoli.

Recovery of blood flow and epithelial layer of the alveoli and tracheal mucosa is accompanied by a significant increase in the transforming growth factor $TGF\beta_1$ in the lung tissue, which may be aimed at stabilizing of changes in the vascular wall, new microvessels differentiation, formation of the extracellular matrix and intercellular connections between endothelial cells. Apparently, the recovery of pulmonary blood flow, vascular permeability and reconstitution of epithelial structures in the recovery period is regulated by the activation of transforming growth factor TGFβ1.

IL-10, IL-4, TNFa in the lung tissue did not differ from the control values. Thus, the fluid shift in the cranial direction was accompanied by a compensatory change in hemodynamics in the respiratory organs (plethora of venous vessels of the lungs, spasm of the walls of arterioles), without pronounced structural and functional disorders of the tracheal wall and lung tissue.

Cytokine regulation of compensatory reactions is accompanied by a significant increase in $TGF\beta_1$.

SPACEFLIGHT-ASSOCIATED CHANGES IN THE PERIVASCULAR SPACES OF ASTRONAUTS AND COSMONAUTS

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Very recently, it was observed that long duration spaceflight is associated with an upward shift of the brain towards the cranium, redistribution of CSF with narrowing of the subarachnoid space at the vertex, crowding of brain tissue along the superior sagittal sinus, and enlargement of the cerebral ventricles.1-3 Continued enlargement of the ventricles has been documented after spaceflight even up to one year after return to Earth in both NASA astronauts and Russian cosmonauts.3

The current study focuses on perivascular spaces (PVS, also known as Virchow-Robin spaces), a brain-wide network of perivascular channels along which a large proportion of CSF (or CSF-like fluid) circulate through the brain parenchyma4, which have not yet been evaluated after spaceflight. Hereto, a comparative, joint quantitative analysis of alterations in cerebral CSF spaces across astronauts and cosmonauts, using the same analysis pipeline thereby eliminating investigators bias, has been performed for the first time in space research history.

We performed a joint analysis of magnetic resonance imaging (MRI) brain scans in 23 National Aeronautics and Space Administration (NASA) astronauts, 13 Roscosmos (ROS) cosmonauts, and 4 European Space Agency (ESA) astronauts before and after long-duration spaceflight (mean: 179.0 ± 48.3 days) on the International Space Station (ISS). An additional follow-up scan was performed in 4 ESA astronauts and 10 cosmonauts 7 months after return to Earth. Brain MRI data from 13 age- and education-matched male volunteers acquired with a time interval similar to the preflight-postflight and preflight-follow-up (n = 8) intervals and from 7 NASA astronauts acquired before and after missions of short duration in the Space Shuttle Program were used as controls.

In these cohorts, we document alterations in PVS volumes, which is a totally new observation. But even more striking, NASA astronauts had a larger increase in PVS volumes than Russian cosmonauts, despite being as long in space. We hypothesize this difference may be related to on-board differences in countermeasure or exercise usage between the American and Russian programs. Additionally, PVS differences between the Russian and American crewmembers could point towards a physiological mechanism underlying spaceflight associated neuro-ocular syndrome (SANS), a condition associated with visual acuity changes and ophthalmological exam findings which is considered a serious medical risk for long-duration spaceflight.5 Our study is the first ever reporting on combined results of brain data from 3 different space agencies.

CONTINUOUS AND INTERMITTENT ARTIFICIAL GRAVITY AS A COUNTERMEASURE TO THE COGNITIVE EFFECTS OF 60 DAYS OF HEAD-DOWN TILT BED REST

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Environmental and psychological stressors can adversely affect astronaut cognitive performance in space. This study used a 6 head-down tilt bed rest (HDBR) paradigm to simulate some of the physiologic changes induced by microgravity. Twenty-four participants (mean ± SD age 33.3 ± 9.2 years, N = 16 men) spent 60 consecutive days in strict HDBR. They were studied in three groups of eight subjects each. One group served as Control whereas the other two groups received either a continuous (cAG) or intermittent (iAG) artificial gravity (AG) countermeasure of 30 minute centrifugation daily (1 g acceleration at the center of mass and 2 g at the feet). The centrifugation protocol included: acceleration at 5°/s^2 for 32–33 seconds until target rotation speed was achieved followed by rotation at constant velocity for either 30 minutes (cAG) or 5 minutes, with a 3minute rest, repeated six times (iAG). Deceleration was at 5°/s^2. Participants performed all 10 tests of NASA's Cognition battery and a brief alertness and mood survey repeatedly before, during, and after the bed rest period. A modest but statistically significant slowing across a range of cognitive domains was found in all three groups during HDBR compared to baseline, most consistently for sensorimotor speed, whereas accuracy was unaffected. These changes were observed early during HDBR and did not further deteriorate or improve with increasing time in HDBR, except for emotion recognition performance. With increasing time spent in HDBR, participants required longer time to decide which facial emotion was expressed. They were also more likely to select categories with negative valence over categories with neutral or positive valence. Except for workload ratings, which were assessed lower in the Control group, continuous or intermittent AG did not modify the effect of HDBR on cognitive performance or subjective responses. Participants expressed several negative survey responses during HDBR relative to baseline, and some of the responses further deteriorated during recovery, stressing the importance of adequate medical and psychological support during extended duration HDBR studies. In conclusion, 60 days of HDBR were associated with moderate cognitive slowing and changes in emotion recognition performance, but these effects were not mitigated by either continuous or intermittent exposure to AG for 30 minutes daily.

Support: NASA through 80NSSC18K0765, German Aerospace Center (DLR).

CHANGES IN CREW COHESION AND HABITAT USE DURING TWO 1-YEAR ANTARCTIC WINTER-OVER MISSIONS

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Exploration-type missions will require humans to live in isolated, confined, and extreme environments (ICE) for prolonged periods of time. Antarctic research stations are considered a high-fidelity ICE analog for long-duration space missions (LDSM). We investigated N = 13 and N = 12 subjects overwintering in the French-Italian Antarctic Concordia station in 2015 and 2016, respectively. During the winter-over, the Concordia crew continuously wore actigraphs (Actigraph Link, Pensacola, FL) that recorded wrist movements and were used to infer activity levels in addition to times spent sleeping and awake. The actigraphs also had a proximity feature, i.e., they were able to detect other devices (either worn by other crew members or strategically placed across the station) via Bluetooth and log the time and signal strength. The proximity feature was used as a surrogate measure of crew cohesion and to investigate systematic changes in crew cohesion and habitat use within and between the 2015 and 2016 winter-over crews. N = 21 crew wore the watch enough during the daytime to contribute to the analysis. With

this technology, we were able to identify systematic changes in crew cohesion with time in mission, which showed a declining trend in the 2015 crew, while the 2016 crew showed lower cohesion overall, but with no significant change with time in mission. Factor analysis was used to identify crew subgroups that spent a lot of time together, how each individual contributed to subgroup and overall crew cohesion, and how the cohesion pattern for each crewmember changed over time. Finally, we found systematic trends in how the facility was used by time of day and across the mission. For example, sensors placed in the gym revealed differences in exercise patterns between individual crewmembers. Overall, this unobtrusive technology provided relevant information both in the social-behavioral and in the sleep-wake domain considered critical for the success of LDSM.

Support: NASA through NNX14AM81G, ESA through AO-13-Concordia, and the German Aerospace Center (DLR).

MICROBIAL MONITORING IN THE EDEN ISS GREENHOUSE, A MOBILE TEST FACILITY IN ANTARCTICA

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The EDEN ISS greenhouse, integrated in two joined containers, is a confined mobile test facility in Antarctica for the development and optimization of new plant cultivation techniques for future space programs. The EDEN ISS greenhouse was used successfully from February to November 2018 for fresh food production for the overwintering crew at the Antarctic Neumayer III station. During the 9 months of operation, samples from the different plants, from the nutrition solution of the aeroponic planting system, and from diverse surfaces within the three different compartments of the container were taken [future exploration greenhouse (FEG), service section (SS), and cold porch (CP)]. Quantity as well as diversity of microorganisms was examined by cultivation. In case of the plant samples, microbial quantities were in a range from 102 to 104 colony forming units (CFU) per gram plant material.

Compared to plants purchased from a German grocery, the produce hosted orders of magnitude more microorganisms than the EDEN ISS plants. The EDEN ISS plant samples contained mainly fungi and a few bacteria. No classical food associated pathogenic microorganism, like *Escherichia* and *Salmonella*, could be found. Probably due to the used cultivation approach, Archaea were not found in the samples. The bioburden in the nutrition solutions increased constantly over time but never reached critical values like 102–103 CFU per 100 mL in irrigation water as it is stated, e.g., for commercial European plant productions. The surface samples revealed high differences in the microbial burden between the greenhouse part of the container and the SS and CP part. However, the numbers of organisms (bacteria and fungi) found in the planted greenhouse were still not critical. The microbial loaded surfaces showed strong temporal as well as spatial fluctuations. In samples of the nutrition solution and the surface, the number of bacteria exceeded the amount of fungi by many times. For identification, 16S rRNA gene sequencing was performed for the isolated prokaryotic organisms. Phylogenetic analyses revealed that the most abundant bacterial phyla were Firmicutes and Actinobacteria. These phyla include plant- and human-associated bacterial species. In general, it could be shown that it is possible to produce edible fresh food in a remote environment and this food is safe for consumption from a microbiological point of view.

SUMMARY OF HUMAN FACTORS BEHAVIORAL PERFORMANCE EXPLORATION MEASURES IN SIRIUS `19

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Long-duration missions beyond Low Earth Orbit will require crews to adapt to extreme conditions including autonomous operations in an isolated and confined environment, variable workload, and separation from family and friends. These challenges can lead to decrements in operationally relevant performance and well-being. The Human Factors and Behavioral Health Exploration Measures (HFBP-EM) is a suite of measures systematically collected in NASA-sponsored analogs to help characterize the spaceflight risks related to behavioral health and performance, determine baseline functioning for individuals and crews in isolation, and assess the efficacy of countermeasures. We collected the HFBP-EM in SIRIUS-19 to assess the operational feasibility and acceptability of the HFBP-EM in the Russian NEK space analog, and to allow for comparisons between longer missions such as SIRIUS-19 with shorter 45-day missions conducted in the Human Exploration Research Analog (HERA) facility at Johnson Space Center. We collected data from 6 participants and multiple mission control members. 6 participants were isolated and confined to the NEK facility for 4-months. The HFBP-EM suite was collected prior to, during, and after the 4-month isolation period. Data were collected on behavioral health, team dynamics, and performance from wearables such as

actigraphy and a heart rate monitor, and daily (e.g., conflict, affect, workload), weekly (e.g., depression, team cohesion), and bi-weekly self-report surveys (e.g., social support). Data on a cognitive task as well as an operationally relevant performance task were collected 1x/week. Mission control provided daily team performance ratings. Results indicated a comparable data yield to data collected in HERA. A summary of results related to behavioral health, team dynamics, and performance over time in the 4-month isolation chamber study will be presented.

RESTRICTED ACTIVITY AND PROTEIN SYNTHESIS IN POSTURAL AND LOCOMOTOR MUSCLES

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With urbanization, automation and mechanization of labor, a difficult epidemiological situation and self-isolation, the level of daily physical activity in a modern person decreases. The aim of the study was to study the effect of restricted activity on protein synthesis in postural and locomotor muscles. An experiment with restricted activity for 21 days was carried out on Wistar rats. The intensity of protein synthesis and anabolic signaling pathways were studied in the soleus muscle (m. soleus), which mainly consists of slow fibers, and the long extensor digitorum of the fingers (m.EDL), mainly consists of fast fibers. The mass of m. soleus and m.EDL was reduced, and a significant decrease in protein synthesis was observed only in m.EDL. There was also a decrease in the phosphorylation of S6 ribosomal protein only in the fast muscle. At the same time, a GSK3β phosphorylation was decreased in m. Soleus, in contrast to m.EDL. Markers of proteolysis have been studied. In the experiment, a decrease in the MuRF-1 expression in m. soleus and Atrogin-1/MAFbx expression in m. EDL was observed, as well as an increase in the expression of calpains in m. soleus. Thus, atrophic processes are associated with restricted activity in fast and slow muscle by different signaling mechanisms.

This work was supported by the Russian Foundation for Basic Research grant #19-015-00074.

THE OPTIMALITY CRITERIA FOR CROP LIGHTING INSIDE PLANT GROWTH UNIT FOR EXTENDED MANNED SPACE MISSIONS

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In the course of long duration interplanetary missions, higher plants will play an integral part in advancing the crew habitat and life support systems (LSS). Initially, the LSS is expected to employ small scale Plant Growth Units (PGUs) to supplement the crew diet with natural vitamin rich fresh vegetables. It is important to optimize the lighting regime inside PGU because luminaries' may consume more than half of the total PGU energy consumption. The lighting optimizing for space PGUs equipped with LEDs lamps requires some quantitative and measurable criterion of optimality. It was proposed (Корбут, 1981) to use optimality criterion for the crop lighting (Q) as maximum of the product:

$$\max Q = \max [m \cdot (m/I)] = \max [m^2 / I], \quad (1),$$

where m – crop dry biomass yield per square meter, I–incident photosynthetic photon flux density (PPFD) during cultivation period, $I_{max} > I > 0$, I_{max} – light saturation threshold of the crop. However, criterion (1) leaves out a probability of different costs for onboard resources (energy power, pressurized volume etc.) in the particular space missions. Another criterion to establish optimal lighting inside space PGU was suggested in the work (Berkovich et al., 2005),

$$\max Q_1 (I) = \max\{[C_v / (C_v + C_E)] M_V(I) + [C_E / (C_v + C_E)] \cdot M_E(I)\}, \quad (2).$$

Here, M_E, M_V are the highest dry biomass yield per unit of the crop lighting power and per volume unit of the plant growth chamber, correspondingly; C_E – cost of consumed by PGU electric power unit; C_V – cost of a volume of PGU; I – lighting attribute which includes combination of parameters (intensity, spectrum, time distribution). Max Q in eq. (2) has meaning of the optimal specific plant productivity per consumed resources.

One weakness of the criterion (2) is indistinct correlation with Equivalent System Mass (ESM) metric which is currently accepted to estimate optimal availability for space life support subsystems (Drysdale, 1998). The less ESM, the better LSS construction. To minimize lighting dependent part of ESM for space PGU we proposed the criterion in form of

$$\min G(t_i) = \min S (A + B I(t_i)) M(t_i) \quad (3).$$

Here G is light dependent ESM; S-illuminated crop area, A and B are the costs of the unit of planting area and the unit of electric power consumed by the luminaries', in kg/m^2 and kg/kW, respectively; I is the incident PPFD; $\delta M(t_i) = k\ F(t_i)$ is the current crop biomass increment in t_i moment, $F(t_i)$ is the current net crop photosynthesis; k is constant. A and B substantially depend on both the spacecraft design and space mission scenario.

We have calculated the coefficients in equation (3) for published scenarios of space missions: LEO mission, Moon planetary mission and Mars planetary mission. The criterion (3) has been used for bench-scale adaptive search of optimal crop lighting during plant growth inside model PGU for extended manned space missions.

SOCIAL RESEARCH IN SPACE AND MILITARY MISSIONS IS THE «HOUSE WITH THREE FLOORS»

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Topic. Presented contribution fits thematically the area of simulated space missions and slightly touches, through a comparative view, real military missions. Both types of «expeditions» involve people of specific professions, performing highly specific work activities in a specific and often extreme work / environment. The common denominator of these expeditions is a highly demanding environment with a potential risk of damage of physical and mental health and danger to life or its loss.

Aim. Purpose of the paper is to present selected key findings from a comprehensive analysis of the attitudes of crew members in the second stage of the project SIRIUS 18/19, which relate to 1. the level of work / life satisfaction, 2. the structure and dynamics of relationships and ties in the crew and 3. specific areas (fatigue, sleep quality, etc.). Highlight «strengths and weaknesses» and make proposals for socio-technical measures.

Method. To uncover and analyze obtained data through social action research, the author's own questionnaire methods were used, verified in common civil and extremely demanding conditions of specific professions within 25 years period that made it possible to describe the level of work / life satisfaction within both simulated flights. The second diagnostic method was Sociomapping, enabling accurate, clear and graphically clear representation of the structure and dynamics of relationships and ties in a given social unit in the form of so-called sociomaps. The methods were deployed in three phases of the experiment – before its start, in its middle and after its completion. One of the methods collected data on the dynamics of relationships and bonds every fortnight of isolation. The implemented methodology made it possible to obtain a comprehensive view of functioning crew from a psychosocial point of view.

Results. The research project of the Czech «KOSMOW» team, analyzing six-member gender-mixed multicultural crew, focused on ten key areas. The outputs show a high level of satisfaction with the work environment, the social atmosphere in the crew team, interpersonal relationships across the spectrum, communication, level of cooperation and overall management of people's activities. On contrary, individual areas of preparation for the experiment were clearly identified for development. Useful and valuable outputs are suggestions and recommendations of the respondents themselves usable in the next stage of the isolation experiment SIRIUS 20/21. Results of this work bring a set of so-called socio-technical measures for the organizers of the isolation experiment (IBMP RAS and NASA), in personnel, psychosocial, organizational, material-technical and professional fields. The benefit of this project is to verify the need to introduce work with the crew team, for example in the form of development workshops, which should always be implemented in the preparatory period before and after the experiment. A proven technique is team coaching using the Sociomapping method, which significantly strengthens the cohesion of the group.

MONITORING PHYSICAL ACTIVITY, PSYCHOLOGICAL, PHYSIOLOGICAL PARAMETERS AND INDEPENDENT OF ENVIRONMENTAL FACTORS IN THE EXPERIMENT SIRIUS-19

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Earlier, in experimental studies simulating the conditions of a long stay of crews in confinment condition with an artificially created habitat (SPINCSS, Mars-105, Mars-500), data were obtained on the peculiarities of the formation of daily and longtime chronobiological rhythms of individual adaptation of the cardiovascular system (CVS) of the volunteers and psychosocial interaction of small groups in confined spaces. Under these conditions, in addition to the factors of direct isolation that affect the heart rate, blood pressure and psychological status of a group of practically healthy people, it is worth considering electromagnetic radiation (EMR), which is commonly called «non-ionizing», which is the same constantly acting environmental factor. The increasing decrease in total motor activity should probably also be attributed to alarming factors, since it not

only provokes a decrease in exercise tolerance, but is also an indicator of mental asthenization. We present the results of studies with the participation of volunteers in a mixed crew: 3 men and 3 women, conducted as part of the international model experiment SIRIUS-19, which reproduces the characteristics of a space flight to the Moon and stay on a lunar base. Part of the scientific program of the experiment included studies of oscillations of non-ionizing radiation, heliogeomagnetic background, electromagnetic radiation and the surrounding ionosphere based on monitoring the hydrogen parameter pH and redox potential (ORP) of the clear water solution. In addition, we studied daily fluctuations in the parameters of autonomic regulation of heart rate (HRV) on weekdays and weekends to determine possible interrelated biotropic effects.

The biorhythmological daily profile of every participant is individual and has the remarkably similar structure during each 24-hour study, while differences and features of the autonomous regulation of body functions in a multi-gender crew are noted. Under the conditions of 4-month isolation, male volunteers showed a greater tendency to a decrease in the average daily heart rate (HR) with each subsequent measurement. According to the dynamics of time and frequency indicators of HRV, one can judge about the strengthening of parasympathetic influences, which also coincides with a decrease in the total volume of motor activity. In addition, daily control of actigraphy showed that an increasing decrease in motor activity in isolation is combined with a change in behavior patterns. The most similar indicators of circadian rhythms were found when recording data with a frequency of 10–12 days. On weekends, the morning increase in heart rate corresponding to the time of awakening is shifted by 1–1.5 hours. The day with the highest level of disturbance of the ionosphere was registered when the maximum activation of the parasympathetic division of the autonomic regulation of the cardiovascular system was registered in the HRV parameters in the time and frequency regions.

The study is supported by the Russian academy of sciences (Themes 64.1, 65.1, 65.2).

THE INFLUENCE OF 8-HOUR'S COMPENSATION OF THE EARTH'S MAGNETIC FIELD ON THE AUTONOMIC REGULATION OF THE HEART

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The planning of manned missions in deep space in the absence of the Earth's magnetosphere obliges us to take seriously the issue of experimental modeling of hypomagnetic conditions (HMC) affecting the human body. The circulatory system (CVS) and the mechanisms of its regulation can be one of the main targets. The issues of creating an artificial geomagnetic field, the safety and reliability of individual means of human protection have not been studied enough. Experiments with human participation sometimes give ambiguous results and are carried out under conditions of limited exposure time.

We have conducted studies with an increased time of exposure to HMC in combination with a factor of limiting physical activity. For the exposition of 8 male volunteers aged (25–35 years) during a continuous 8-hour exposure, the «Arfa» installation was used, in which HMCs were created with an average 1000-fold attenuation in the group relative to the Earth's magnetic field. The studies were carried out twice under the conditions of HMC and an imaginary exposure - placebo (PLB), while all participants in the experiment at the time of exposure were not notified of the presence or absence of HMC. The human cardiovascular system was used as the object of the study based on the analysis of indicators of autonomic regulation of the heart rate. The analysis of 24-hour monitoring ECG data was carried out using portable Holter and specialized software with the calculation of indicators of heart rate variability (HRV). When analyzing the data, both of individual's and the data combined into a group, according to the average hourly HRV indicators, tendencies were outlined that characterize the increase in the activity of the regulatory links of the parasympathetic division of the autonomic regulation of the heart.

The use of the ANOVA technique with repeated measurements, in which every 5-minute fragments were analyzed step by step, revealed significant differences in most HRV indicators (lower HRV with $p < 0.0001$). The heart rate decreased (63.6 ± 0.1vs 56.8 ± 0.3 bpm), while the total HRV reflected by the SDNN components significantly increased (87.3 ± 1.1 vs 130.7±4,1 ms) and TP (6.08 ± 0.1 vs 11.2 ± 0.6 ms2). Sympathetic addressing to the heart, assessed by the Stress Index (by Baevsky's), significantly decreased from 45.9 ± 0.9 vs 22.3 ± 1 c.u. and the LF/HF ratio (2.9 ± 0.1 vs 1.8 ± 0.1). There was significant vagotonic activation: RMSSD (47.9 ± 0.2 vs 63.3 ± 0.9 ms) and pNN50% (26.8 ± 0.2 vs 38.6 ± 0.6), as well as an increase in HF spectrum (0.8 ± 0.02 vs 1.06 ± 0.04 ms2). It should be noted that only with HMC (cross-correlation analysis) there was an increase in the entropy of HRV indices with the appearance of components of the «complexity» of autonomous regulation of the sinus node of the heart. Stress physiological response should activate the sympathetic branch of autonomic regulation. Regarding HRV indicators, this is a decrease in variability, a decrease in the power of the frequency components of HRV, which is a hallmark of «decreasing system complexity». From the results obtained, it follows that adaptation to HMC occurs due to a significant increase in the activity of the parasympathetic (vagal) link in the regulation of heart rate, a less costly adaptive process. On the other hand, the presence in the group of healthy subjects of a representative with an extremely high vagal tone (a trained athlete), in whom the effect of HMC caused a slight inversion of regulatory mechanisms towards sympathetic activation, indicates the presence of a «phenomenon» of adaptation to HMC.

The study is supported by the Russian academy of sciences (Themes 64.1, 65.2).

SPACEFLIGHT DURATION AND THE MORTALITY OF COSMONAUTS

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Introduction. On 25.12.2020 FMBA of Russia approved the Concept for the Development of Space medicine until 2030 (Order N392), according to which the major pillar of development is the scientific basis of establishing the cosmonauts' health monitoring system throughout their life to determine the effects of spaceflight factors on the human body in the distant period. Assessing the real effects of the spaceflight factors on the cosmonauts' health in the distant period may be complicated by the "healthy worker" effect as a result of careful medical selection process.

The goal of this work is to study the mortality of cosmonauts with spaceflight experience as the most informative health indicator in the distant period.

Methods. A cohort epidemiological study was conducted, 118 Soviet and Russian male cosmonauts with spaceflight experience formed a cohort. The follow-up period was 59 years (01.01.1960-31.12.2018) with 3867.5 person-years obtained.

Results. 37 cosmonauts died by the end of follow-up, all deaths were among persons enlisted in the groups before 1989, the mean age of death was 64.4. 48.65% died due to cardiovascular diseases (I00-I99), 27.03 % died of malignant neoplasms (C00-C97), 16.22% died from external causes (V01-Y98), 5.41% had other causes of death, 1 cause of death (2.7 %) is unknown.

Deceased cosmonauts spent the least time in space among all persons enlisted before 1989 (2155 days out of 14749). Moreover, spaceflights were made mainly in the early stage of space exploration when their duration was relatively short.

Discussion. Considering that all observed deaths occurred in cosmonauts who were enlisted in the groups before 1989 and were under the influence of spaceflight factors for a relatively short time, there is a need for more research on the effects of spaceflight factors on cosmonauts' health in the distant period.

The reported study was funded by RFBR, project number 19-315-90023.

THE ROLE OF AI POWERED AUTONOMOUS AVIONIC SYSTEMS IN INTERPLANETARY SPACEFLIGHT

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In aerospace engineering, avionics plays a crucial role in defining the successful flightpath, right from the juncture of take-off to the landing. Avionics is often integrated with software communication systems on airplanes, satellites, spacecrafts, rockets and other experimental space vehicles for bringing off the quintessential performance outcomes in the form of smooth, safe and successful aerodynamic response and operation. The flight-control avionic systems of the present generation aircrafts feature an autonomous function, commonly called the autopilot mode for executing a consistent flight potency. A certain amount of autonomy in avionics had been in use for decades, but the recent trends have started to showcase the slow implementation of onboard devices that mimic basic human cognizance and are thus characterized by Artificial Intelligence. The manufacturers and organizations, these days, are focusing on the integration of autonomous features in avionic systems and the upgraded software-based data-collecting devices that as amalgamated units are capable of mimicking intelligence quotient, parallel to the human brain, representing some basic levels of AI elements. The future desideratum for adapting AI into avionics is essentially for aiding pilot workload, handling of emergency situations, detecting and rectifying faults, conditioning of safe human environment and aerodynamic stabilization conditions. The commonly interdependent factors to AI being Virtual Reality and Machine Learning may demonstrate the conglomerated outcome where AI, VR and ML work in an efficiently concomitant scenario for corroborating the true sense of AI. The important considerations of integrating Artificial Intelligence with onboard avionic systems, relevant in space explorations, are discussed and analyzed for recognizing the previously unknown factors and determinants that may be crucially impacted through AI networked computers in the future spaceflight missions. Such considerations may also prove useful in creating and safeguarding the mimicking features in AI housed packages for the onset of successful interplanetary spaceflight operations.

STRUCTURAL AND FUNCTIONAL EFFECTS OF FULL-BODY SPACE RADIATION EXPOSURE ON THE RIGHT VENTRICLE AND LUNGS

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During future exploration-type space missions, astronauts could be exposed to doses of space-type radiation (IR) from galactic cosmic rays (GCR). Emerging evidence suggests that space-type IR may alter the cardiac and vascular cell function by modulating various molecular mechanisms in the heart and lungs. However, the long-term effects of space-type IR remain largely unknown in the lung and right ventricle (RV). Here, we aim to characterize the structural and functional consequences of full-space radiation exposure on the RV and lung tissue in wild-type (WT) and ApoE knock-out (ApoE-/-) mice.

Our results showed that a single exposure to body gamma irradiation (γ-IR 100 and 200 cGy) and 5-Ion Simplified GCR simulation (simGCRsim 50, 100, and 150 cGy) potentiated the mRNA expression of proliferation, oxidative stress, inflammation gene markers at 28-days post-IR exposure. Further histological analysis of hematoxylin and eosin- and Masson's trichrome-stained lung tissue revealed a significant increase in vascular remodeling of distal pulmonary arteries and perivascular fibrosis after both types of IR. Interestingly, we also noticed a significant perivascular inflammatory infiltration and perivascular after simGCGsim radiation. Additionally, direct cardiac hemodynamic measurement by right heart catheterization showed higher right ventricular systolic pressure (RVSP) after exposure to γ-IR 200 cGy or simGCRsim 100 cGy in ApoE-deficient mice at 12-months post-IR, which was associated with exacerbated vascular remodeling and lung fibrosis. RV echocardiography and vascular doppler analyses revealed a significant increase in RV internal dimensions at systole and diastole (RVIDd and RVIDs) in ApoE-/- at 22-months after IR exposures. WT mice showed a 2-fold decrease in RV diameter at mid-level after exposure to all doses and types of radiation. We did not found any significant changes in RV wall thickness in diastole (RVWthd). Interestingly, we found an increase in the pulmonary artery diameter and pulmonary valve maximum velocity in WT and ApoE-/- mice exposed to 50 cGy simGCRsim and 200 cGy γ-IR.

In conclusion, the early changes in expression of the proliferation, inflammation, and oxidative stress markers along with the structural and functional alterations observed at 12 and 22 months suggest that gamma- and simGCRsim-IR may trigger the onset of pulmonary arterial hypertension in long-term studies.

BIOLOGICAL RISKS AND ITS IMPLICATIONS FOR CREWED INTERPLANETARY MISSIONS

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In this paper, we have emphasized the major space challenges such as microgravity, space radiation and temperature, vacuum environment, bio-wastes, habitat and life support system, improper sleep patterns, food preservation, psychological issues and nuclear hazards. In addition to this, we have discussed the biological risks associated with these challenges along with its countermeasures. Our analysis is based on the study and perspective of a crewed mission to Moon, Mars and beyond. Further, the bio-risks highlighted here are the effect of osteoporosis, abnormal vision, orthostatic hypo or hypertension, fluid distribution, changes in brain positions due to microgravity; prolonged cancer, sterility, cataracts, cardiovascular disease, acute radiation syndrome due to radiation; bubble formation and physical damage due to vacuum environment; the effect of hypothermia and frost formation due to low space temperature; oxygen and breathing-related issues due to challenging habitation; damage of circadian rhythm, sleep deprivation and metabolic disorder due to improper illumination and sleep patterns; food poisoning, growth of fresh fruits and vegetables and their impact on psychological health; and the effect of nuclear radiation in case of nuclear propulsion systems. Furthermore, the study shows effective countermeasures as artificial gravity and regular exercise for microgravity, fabrication of materials using polyethylene and hydrides to shield from radiation, proper disposal procedure using anaerobic digester for bio-wastes, a light sensor to induce sleep thereby generating illumination environment, and growth of fresh fruits and vegetables aboard space vehicle to improve psychological health issues.

VIRTUAL REALITY BASED SIMULATOR TRAINING FOR POTENTIALLY DANGEROUS AND LIFE CRITICAL EMERGENCY REHEARSALS

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Simulator based training is a widely used approach till now for crew training in aviation as well as in human spaceflight missions. While this is useful in many circumstances, training for all potential hazard-ous scenarios is not possible as it is

difficult to safely simulate the hazardous situation. Moreover, simu-lating various scenarios requires extensive facilities and infrastructure to be set up which is a capital in-tensive and time consuming activity. Physical simulators often work within rigid simulation protocols and it becomes prohibitively costly to introduce any variation to improvise training.

Training in Immersive Virtual Reality (VR) is an innovative approach that is being implemented in a va-riety of training and demonstration activities. Review of literature shows that, in the areas of medical re-search, equipment design, troubleshooting, product demonstration are some of the areas where VR train-ing has proven useful. This technology uses a wide field of view with interactive options to allow the user to interact with the virtual world in high resolution simulated visual and auditory scenarios. VR training was used in training of operating room fires, construction site safety, disaster drills and mining accidents training due to its immersive nature and yet virtual environment. The common feature of all of these is that, it is difficult to realistically simulate these scenarios in most physical simulators.

Some of the dangerous yet critical emergency scenarios that can be safely simulated in a VR envi-ronment can be simulated by tailoring the virtual environment to cover all contingencies. This paper dis-cusses the framework for VR based astronaut training using typical spaceflight scenarios. The paper also proposes VR training approach for scenarios where physical simulation has been used pervasively till now. This VR based training protocol will be beneficial for future human spaceflight endeavours when space travel will expand massively and hence, would require cheaper and efficient means for training the crew.

AI BASED CLASSIFICATION ALGORITHMS TO IDENTIFY WARNING SIGNS DURING CONTINUOUS MONITORING OF PHYSIOLOGICAL PARAMETERS

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Medical monitoring and intervention is an integral element of any human spaceflight mission man-agement protocol. This is applicable for human spaceflight missions to low earth orbit / near earth planetary bodies where real time communication is possible. There is also an emerging need for robust autonomous health monitoring and diagnosis systems for future missions where communication latency will be an issue.

Continuous monitoring of physiological data that are acquired hundreds of times per second is a humungous task even for a trained medical personnel manning the mission control centre console. Even with pre-processing, the data monitoring in real-time for a short duration mission is taxing for the medical personnel. Data processing and preliminary interpretation is therefore relegated to software based algorithms to process and provide preliminary interpretation of data to the medical personnel.

This paper discusses the current AI based algorithms that can be used for feature extraction fol-lowed by classification of time-domain physiological data. The use of Convoluted Neural Networks (CNN) which are widely used in image processing in medical diagnostics have inherent problems when dealing with sequential data that changes over time. There has been recent research on use of Recur-rent Neural Networks(RNN) and Long Short Term Memory (LSTM) networks either individually or in com-bination for classification of time domain data. The accuracy in classification for ECG data has been reported to be as high as 95–97 %.

This paper proposes the use of AI based algorithms for classification of continuous physiological signals into normal and abnormal. The sensitivity and specificity of such a classifier required to act as a robust threshold for drawing attention of the human observer is also discussed.

THE WATER MANAGEMENT ON PROSPECTIVE SPACE STATIONS

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The implementation of advanced orbital and interplanetary manned flights depends on the perfection of the crew's life support systems (LSS). One of the key components of the LSS is a group of water supply systems (SVO). Due to energy, volume and mass constraints LSS based on physical-chemical processes will be used on space stations in the foreseeable future. The use of biological processes and food production is the aim of the future. Probably a vitamin greenhouse will be used.

Based on the experience of life support of space orbital stations, the structure of a promising complex of physical-chemical life support systems was formed. If oxygen is obtained by electrolysis of water, the closure of the LSS complex is determined by the water technical balance. Therefore, a group of water supply systems should regenerate water from all water-containing waste products with a maximum water recovery coefficient and minimal mass and energy consumption, ensuring minimum

water consumption from reserves. For a group of atmospheric regeneration systems, the principal closing element is the extraction of oxygen from carbon dioxide.

The choice of water regeneration processes is determined by the contamination of water-containing products. The following processes are currently using: sorption-catalytic and electrochemical purification for humidity condensate, urine distillate, transpiration moisture from a vitamin greenhouse, condensate from a waste treatment system; distillation for recovery water from urine preserved with chemical reagents; multi-stage filtration and reverse osmosis for sanitary and hygienic water; drying of dense waste with sorption-catalytic purification and decontamination of condensate; pasteurization and introduction of ionic silver for decontamination of food water. The analysis shows that the listed chemical and technological processes will be used in promising systems with increase of waste-free electrochemical processes using. In addition, it is necessary to develop a universal backup process for water regeneration in case of failure of the regular systems.

The equipment of advanced water regeneration systems shall undergo significant modernization. The main factor is an increase in reliability and an in the service life and the resulting reduction in mass consumption. The specific mass consumption (kg per kg of recovery water) should be reduced in some times. The largest contribution to mass consumption is made by water reserves determined by the unbalance of water. Therefore, the water extraction coefficient should be maximum. The mass consumption of the system should be calculated taking into account its contribution in the unbalance of water. Water regeneration systems have relatively low energy consumption; however, one of the directions of development is to further reduce this parameter. A mandatory requirement is to check the advanced equipment and processes on the ISS.

The above aspects of water management are illustrated in the report based on the experience of water management of the ISS Russian segment.

INTER-INDIVIDUAL AND INTRA-INDIVIDUAL VARIATION OF SPACEFLIGHT-INDUCED MUSCLE ATROPHY: RESULTS FROM THE EDOS-2 STUDY

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During long-term exposure to microgravity multiple musculoskeletal as well as cardiovascular adaptations of the human body including muscular wasting could occur. Due to lower loads of the anti-gravity muscles, especially the lower extremities are affected. To maintain a high level of musculoskeletal fitness, Cosmonauts and Astronauts perform daily exercises. Individual training responses and muscle adaptations are additionally influenced by parameters like body constitution, nutrition, training stimuli and training responses. During our EDOS-2 study we investigated the muscular loss during the long-term space missions despite intensive, high-volume training activities.

Twelve Cosmonauts and Astronauts were examined pre- and post-flight. Two baseline measurements (B-90 and B-45) and three post-flight measurements (R+1, R+14, R+90) at Tibia 38% and Tibia 66% were performed. Data acquisition was performed with a peripheral quantitative computer tomography (pQCT). As a parameter for muscular wasting we used the cross-sectional area (CSA) at the two body sites. Percent change (pc) defined as the difference of the post-flight result and the baseline measurement divided by the baseline result was analyzed. Furthermore, we analyzed the correlation by using the Spearman correlation coefficient between the body sites. These results were compared to muscular adaptations after two month of bed rest without any intervention during our AGBRESA study, where we measured the CSA at Tibia 66 at B-13 and BR60.

Repeated measures ANOVA indicated significant differences between the study days for both measurement sites ($p<0.001$), and contrast testing showed significant losses R+1 as well as R+14. Notably, there was no difference between baseline and R+90. The results of the pc showed an overall decrease of 13.6% (± 5.3) from baseline to R+1 and of 6.4 % (± 4.6) from baseline to R+14 for Tibia 38, respectively. For Tibia 66, the results were -12.7 % (± 5.4) at R+1 and -6.4 % (± 4.3) at R+14. In comparison, the pc of CSA at Tibia 66 during two month of bed rest was about -21.0 % (± 4.5) till BR60. The results for pc of baseline to R+1 showed that the individual pc for Cosmonauts and Astronauts ranged from -22.7 % to -5.4 % at Tibia 38 and from -24.4 % to -5.7 % at Tibia 66, respectively. The range during AGBRESA was from -27.5 % to -14.7 % from baseline to BR60. The correlation coefficients for pc at Tibia 38 and Tibia 66 during EDOS-2 were for R+1 at 0.8, R+14 at 0.6 and R+90 0.3.

Despite daily activities, these results indicate sustained muscle wasting during long-term space missions. These results showed, that the muscular wasting of a long exposure to microgravity (about 6 month) is comparable to adaptations during two month of bed rest without any intervention. The adaptation at Tibia 38 and Tibia 66 showed a high correlation indicating little intra-limb variation.

SKELETAL MUSCLE ATROPHY IN DISUSE AND MICROGRAVITY: CELLULAR AND MOLECULAR ANALYSES ON MICE AND HUMAN MODELS

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Microgravity has a dramatic impact on most organ systems. We studied structural, functional and proteomic adaptations of skeletal muscle and the underlying cellular and molecular mechanisms induced by spaceflight in humans and by simulated microgravity both in humans, bed rest (BR) and unilateral lower limb suspension (ULLS), and in mice, hindlimb unloading (HU).

As expected, in both human and mice models we found: a shift of fibre type distribution towards fast fibres, a decrease in muscle fibres ad whole muscle cross-sectional area (CSA), and a disproportionate loss of force compared to size, i.e., a decrease in specific force, of single muscle fibres. Proteomic analysis (i.e., 2D gels) of human vastus lateralis (BR & ULLS) showed a downregulation of all myofibrillar proteins. Lower myosin concentration was found in individual human muscle fibres following both BR and ULLS, paralleling specific force loss. Consequently, a decrease in the number of myosin heads interacting with actin at any given time during contraction could play a major role in specific force loss.

We addressed the mechanism causing muscle proteins loss by 2D proteomic and intracellular signalling pathways analyses. In human bed rest and mice HU, we observed: upregulation of NRF2, a transcription factor sensing reactive oxygen species (ROS) in the cell; adaptations of major ROS buffering systems (e.g., SOD, catalase, peroxiredoxins, Hsp); protein oxidation. Such findings were consistent with a potential role of redox imbalance in causing muscle wasting as suggested by several previous findings. To test such hypothesis, we administered trolox, a potent antioxidant, to HU mice. Importantly, NRF2 was not upregulated and no protein oxidation was found, indicating that redox imbalance was prevented by trolox. However, expressions of MuRF-1 and atrogin-1, major ubiquitin ligases of the ubiquitin proteasome system, were still up-regulated and muscle atrophy was not prevented by trolox. Therefore, redox imbalance was not likely to cause muscle atrophy, at least in mice.

Importantly, in human BR and ULLS and in mice HU, proteomic analysis indicated downregulation of both aerobic and anaerobic metabolic enzymes, i.e., a general derangement of energy metabolism.

In human BR and mice HU, PGC1α, an activator of transcription controlling mitochondrial dynamics and biogenesis and inhibiting the ubiquitin proteasome system, was downregulated and expression of proteins involved in mitochondrial dynamics was altered. On such ground, we hypothesized that a metabolic program of muscle atrophy could be activated in disuse. To test such hypothesis, we subjected transgenic mice selectively overexpressing PGC1α in muscle to HU. In both soleus and gastrocnemius muscles of such mice, no upregulation of atrogenes expression was observed following HU and muscle atrophy was almost completely prevented confirming a major role of a metabolic program in disuse muscle atrophy. Using the same approaches, we performed a pilot study on two astronauts who spend 6 months in space. Findings will be discussed with respect to other models.

HEAD-DOWN TILT POSITION, BUT NOT THE DURATION OF BED REST AFFECTS RESTING STATE ELECTROCORTICAL ACTIVITY

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The abstract is based on work that was recently published here: Brauns et al. Front Physiol (in press).

Adverse cognitive and behavioral conditions and psychiatric disorders are considered a critical and unmitigated risk during future long-duration space missions (LDSM). Monitoring and mitigating crew health and performance risks during these missions will require tools and technologies that allow to reliably assess cognitive performance capability and mood states. Electroencephalography (EEG) has the potential to meet the technical requirements for the use during LDSM. Weightlessness is associated with a fluid and brain shift and these effects could potentially confound EEG recordings. Head-down tilt bed rest (HDBR) provides a unique spaceflight analog to study these effects on Earth. Here, we present data from two long-duration HDBR experiments, which were used to systematically investigate the time course of resting state electrocortical activity during prolonged HDBR. EEG spectral power significantly reduced within the delta, theta, alpha, and beta frequency bands. Likewise, EEG source localization revealed significantly lower activity in a broad range of centroparietal and occipital areas within the alpha and beta domain. These changes were observed shortly after the onset of HDBR, did not change throughout HDBR, and returned to baseline after the cessation of bed rest. EEG resting state functional connectivity was not affected by HDBR. The results provide evidence for a postural effect on resting state brain activity that persists throughout long-duration HDBR,

indicating that immobilization and inactivity per se do not affect resting state electrocortical activity during HDBR. Our findings raise an important issue on the validity of EEG to identify the time course of changes in brain function during prolonged HBDR and highlight the importance to use a common body posture during all recording sessions, including baseline and recovery.

The study was sponsored by ESA, and supported by DLR through grants 50WB1525 and 50WB1915.

EFFECTS OF TWO MONTHS OF BED REST AND ANTIOXIDANT SUPPLEMENTATION ON ATTENTIONAL PROCESSING

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Physical inactivity across the lifespan is a growing public health concern affecting the cardiovascular, musculoskeletal, and central nervous system. There is increasing evidence that physical activity enhances cognitive function, promotes mental well-being, and supports psychological health. However, data on the effects of dietary antioxidants as a neuroprotective treatment when physical activity levels are impaired are lacking. In this randomized controlled study twenty healthy men between 20 and 45 years underwent 60 days of bed rest. Participants were randomly assigned to a control group or a treatment group. The treatment group (N = 10) received a daily antioxidant supplement consisting of polyphenols, omega-3 fatty acids, vitamin E, and selenium. No supplement was provided to the control group (N = 10). Event-related potentials (ERPs) and behavioral data from a three-stimulus oddball paradigm were collected eight days before bed rest, after 60 days of immobilization, and after eight days of recovery. To investigate the impact of prolonged physical inactivity with and without antioxidant supplementation on attentional processing, we assessed the change in electrocortical activity and task performance from baseline in response to bed rest in the treatment relative to the control group. After two months of bed rest, we found a significant decrease in task efficiency irrespective of the treatment. These findings were corroborated by lower ERPs in fronto-central and parietal brain regions. Neither behavioral nor electrocortical data returned to baseline values after eight days of recovery. Our results provide support for the adverse and persistent neurobehavioral effects of prolonged bed rest, which could not be mitigated by antioxidant supplementation. These findings raise important implications for situations in which physical activity levels become severely restricted such as medical conditions or sedentary lifestyles.

The study was sponsored by NASA and supported by DLR through grants 50WB1525 and 50WB1915.

EFFECTS OF SHORT-TERM ISOLATION AND CHRONIC SLEEP DEPRIVATION ON COGNITIVE PERFORMANCE

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Long-duration exploratory space missions expose humans to unique stressors including isolation, sleep loss, and high workload that may compromise physical and psychological health and performance. We here investigated the effects of isolation and confinement with and without chronic partial sleep deprivation. Data were collected as part of NASA's HERA campaigns C3 and C4, comprising a total of eight missions, and crews of four subjects (N = 32, 13 women, mean age 38 ± 8). HERA missions of campaign 3 comprised 30 days, whereas the missions of campaign 4 encompassed 45 days. As part of campaign 4, participants were exposed to a partial sleep deprivation during the course of their isolation phase permitting them to sleep for 5h/night on workdays, recovery nights of 8h/night on weekends. We assessed decision making, and multi-task performance using a self-programmed, computer-based set of tests, i.e., the clock task (CT) and a dual task paradigm (DTP). Data was collected in the morning once before mission (7 and 11 days prior to ingress for campaign 3 and 4, respectively); during the mission on days 14 and 28 for campaign 3, and mission day 45 for campaign 4; and one week after egress. Whereas there were considerable practice effects for both tasks in C3, we observed a deterioration in task performance for C4. In particular, 45 days of isolation were associated with a noticeable decrease in performance for the dual and single tasks of the DTP compared to pre-mission and small changes in accuracy and reaction time for the CT. For both tasks, performance was above baseline level one week after the isolation. Our results highlight the risk of potential adverse neurobehavioral effects associated with isolation and chronic sleep deprivation, and the need for target-specific strategies and countermeasures addressing these risks during future exploratory space missions.

The study was sponsored by NASA and supported by DLR through grant 50WB1525 and 50WB1915.

LIFETIME RISK OF TUMOR DEVELOPMENT IN C57B1/6J MICE EXPOSED TO A SINGLE FULL BODY GAMMA AND simGCRsim RADIATION

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Radiation-induced cancer is a primary risk associated with exposure to space radiation (IR) during deep-space missions. There is limited data in humans and in animal models for high charge and energy (HZE)-induced carcinogenesis over lifetime. We hypothesize that exposure to space-type IR may increase risk of cancer development, especially in association with aging processes later on in life.

As part of our NASA-funded mouse-lifetime studies to evaluate the effect of space-type and gamma IR on cardiovascular disease development, mice were systematically examined for tumor development during scheduled tissue collections over 22-months after initial IR exposure. 3-month-old male ApoE null and C57B1/6J wild-type (WT) mice were irradiated with 100 cGy, 0.662 MeV of 137Cs gamma-IR (γ-IR) and 50 cGy, 500 MeV/n of 5-ion simplified GCR simulation (simGCRsim). Control ApoE null and WT mice were fed with mouse chow (normal diet-ND) and Western diet (WD) without radiation. Note, all irradiated mice were fed with a ND for 22 months. All neoplasms were fully bisected with visibly unaffected tissue. Formalin-fixed tissues were submitted for routine H&E staining and evaluation by a pathologist blindfolded to treatment conditions.

At all time points and treatment conditions examined, total of 9 neoplasms were detected in ApoE null. Therefore, we focused our studies on WT mice only. No neoplasms were detected in ND-fed WT mice at 12 and 16 months, and only 1 lymphoma was detected at 22-months. In WT mice, the prevalence of neoplasms was the highest in no-IR, WD-fed mice with 9/15 (60%) and 7/17 (41 %) animals developing neoplasms at 16 and 22 months, respectively. A small number of WD-fed and 100 cGy γ-IR mice developed more than one tumor. At 16 months, tumors in WD-fed mice were represented by 7 liver tumors (2 – hepatocellular carcinomas, 1 – hemangiosarcoma, 4 – metastatic lymphomas), 1 lung (lymphoma), and 1 spleen (hemangiosarcoma) tumors. In WT-IR mice, higher tumor prevalence was found in 100 cGy γ-IR mice 2/16 (12.5 %) and 8/16 (50 %) at 16 and 22 months, respectively, compared to 1/15 (6.7 %) and 6/15 (40 %) tumors in 50 cGy simGCRsim-IR WT mice. The incidence of hepatic and splenic tumors was higher in all groups and was represented by various cancer pathologies – hemangiosarcoma, hepatoblastoma, early carcinoma, lymphoma, hepatocellular carcinoma, histiocytic sarcoma.

In summary, we report here that – i) the incidence of tumors is higher in WT compared to ApoE null mice after the same doses of γ- and simGCRsim-IR suggesting underlying genotypic variance may attenuate pathways involved in tumorigenesis; *ii*) the highest number of tumors during the lifetime of WT mice was detected in the WD-fed group, *iii*) in WT mice, the incidence of IR-induced internal organ tumors was higher in 100 cGy γ-versus 50 cGy simGCRsim-IR, suggesting higher carcinogenic potential of γ-IR at these doses; *iv*) the liver is the most affected organ by tumor growth, followed by the spleen. These results suggest that age-related metabolic changes and IR-induced mutagenesis may drive carcinogenesis. Additional studies are underway to determine the underlying molecular mechanisms involved.

DEVELOPMENT AND INTEGRATION OF A SPACE-FLIGHT SIMULATOR FOR THE SIRIUS ANALOGUE MISSION: SIMKSILL-RU AND SIMSKILL-VR

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Within the framework of the SIRIUS Analogue Mission experimental campaigns in Moscow, Russia, a spaceflight simulator developed by the Institute of Space Systems of the University of Stuttgart has been integrated into the NEK-Facilities of the IMBP. Realistic piloting simulation of the future Russian spacecraft Orel is simulated, and a series of approach and docking manoeuvres to the Lunar Gateway (LOP-G) are proposed. This paper initially discusses the development steps for the implementation of the hardware and software concepts proposed. Then, a first ssessment of the gathered piloting datasets from the SIRIUS-19 Crew (4-Month isolation campaign) is presented. Lastly, the simulation hardware and software upgrades for the implementation of a Virtual Reality simulator on the upcoming SIRIUS-21 8- and 12-Month campaigns are presented and their benefits are briefly discussed.

SPHINGOLIPIDS TAKE PART IN REGULATION OF MUSCLE PLASTICITY DURING GRAVITATIONAL UNLOADING

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Space flight leads to substantial atrophy of skeletal muscles (especially postural) and abnormalities in muscle functions. In a ground-based model of microgravity (hindlimb suspension, HS), we have shown that unloading is accompanied by a number

of alterations indicating the involvement of bioactive sphingolipids in the development of muscle adaptation / disadaption during disuse (Bryndina et al., 2014, 2018, Petrov et al., 2019).

The experiments were performed on male Wistar rats subjected to HS of different duration (12 h, 4 and 14 days). Rats were divided into the following groups: control, HS + vehicle (0.9 % saline), HS + clomipramine (an inhibitor of acid sphingomyelinase, aSMase). SDS/PAGE – WB analysis was applied to estimate the levels of aSMase and nSmase catalyzing the hydrolysis of sphingomyelin; TLC was used for detection of ceramide and sphingomyelin amounts; the changes in muscle phenotype was studied using RT-PCR method and IHC analysis of MyHC isotypes in soleus muscle sections. Ceramide and SMases were determined in detergent resistant membrane fraction (DRM), biochemical analogue of lipid rafts. Muscle atrophy was estimated according to changes in muscle mass and morphology.

We have shown a number of alterations caused by disuse in the soleus muscle: 1) ceramide accumulation was detected throughout the muscle fibers, but preferentially in the sarcolemmal regions including neuromuscular junctions; 2) HS led to the formation of ceramide-enriched membrane microdomains (CEMD) merged into the large platforms known to cluster membrane-bound proteins; 3) high expression of ceramide, aSMase and nSmase found in DRM indicated the involvement of sphingomyelinase hydrolysis in disuse-induced CEMD formation; 4) the rearrangement of caveolin-3/dystrophin-glycoprotein complex was also found. Clomipramine prevented or attenuated aSMase/ceramide upregulation with concomitant diminution of the changes in subsarcolemmal cytoskeleton. The inhibitor also affected the altered expression of MyHC caused by 14-day HS and muscle atrophy. The results obtained indicate the involvement of SMase-dependent mechanisms in the development of disuse-induced muscle alterations.

This work was supported by RSF (grant #16-15-10220) and RFBR (grant #19-315-90099).

USE OF VIRTUAL REALITY TECHNOLOGIES IN THE PROCESS OF MEDICAL AND PSYCHOLOGICAL SUPPORT OF INTERPLANETARY EXPEDITIONS

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The paper deals with the issues of medical and psychological support of manned interplanetary flights. The analysis of the features of their implementation and the risks associated with the human psyche showed that the key feature is the absolute autonomy of the crew's functioning, and the inability to communicate with ground-based flight control services in real time. The need for independent operational decision-making in the event of abnormal and emergency situations against the background of monotonous work, and in certain periods of flight and its complete absence. As one of the directions of medical and psychological support in such conditions, the use of neurocognitive technologies using the means of a controlled virtual environment is proposed. So, at the stage of the crew's flight to the final destination (a station in lunar orbit, the surface of the Moon), the use of virtual reality modeling tools will allow filling the destabilizing information deficit of the crew members with interesting creative work. This will be a unique and much-needed energy for astronauts to achieve results that are satisfying and stimulating in difficult conditions of autonomous flight. It is proposed to use a set of tools aimed at compensating for the negative effects of prolonged stay in an artificial environment, isolation, restriction of external impressions, monotony of the situation and separation from the usual society. It should be taken into account that music, books, entertainment will not save you from experiences, homesickness, the uncertainty of flying in the cosmic abyss, a sense of doom. We need classes «for the head and hands», not invented, not imposed, but proposed based on the needs of the cosmonaut himself, those that were laid down in childhood and later developed by his own efforts, as well as professionally oriented and motivated. In interplanetary flights, the whole complex of medical and psychological support measures should provide: the possibility of creating a controlled virtual environment on the spacecraft to saturate the life of crew members with comprehensive impressions (audio-visual, tactile, etc.). Being a product of information and psychological technologies, the virtual environment will allow you to create controlled situations in flight, both unreal and «earthly» world. Plastically change the parameters of objects and events occurring with them, imitate visual, tactile and auditory images at the same time. Separately, it should be noted the psychotherapeutic capabilities of virtual reality tools. At the level of detailed modeling of three-dimensional reality, they allow you to simulate the presence of a person in a professional and everyday environment. This is especially valuable for an astronaut who is acutely experiencing the phenomenon of «separation from the Ground» in an autonomous long-term flight, in which there is a possibility of reducing the working motivation and overall activity of the crew.

SIGNIFICANT (IN DOZEN TIMES) ATTENUATION OF GAMMA-RADIATION INDUCED DSDNA DAMAGE AT -195.8 TEMPERATURE EXPOSURE

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Introduction. The dsDNA molecules are relatively stable but could quickly degrade/fragmented by ionization radiation. If we are looking for extraterrestrial life (at least on different bodies – planets and their satellites, of our Solar System), the best place to search for it is icy satellites (e.g., Jovian Europa or Saturn's Enceladus) along with polar ice caps on 'atmosphere-lost' Mars. However, the fluxes of highly energized protons (mostly), electrons (mostly for Europa; the surface 1cm deep irradiation – 30kGy/year) and heavy ions on these targets from the parent body (e.g., Jupiter) or cosmic radiation can provide a challenge for DNA (microbial) integrity.

Objectives. The objective of the study was to estimate the low bound of already-known attenuation effect of ultralow temperature at normal pressure on the efficacy of gamma-radiation in braking/fragmenting dsDNA. The general purpose of the study was to simulate the 'fate' of ocean-below-ice-inhabiting microbes flushed out via cracks on the Jovian Europa – how long their DNA inside the cells could withstand the surface radiation fluxes.

Material and methods. As a model, the plasmid vector pCR-4 (~4000bp) for cloning containing the insert of a bacterial rRNA gene (v3-v4 region – 485bp) was used in irradiation trials under the liquid nitrogen conditions (-195.8oC). The gamma-induced fragmentation was tested in specific PCR generating the dsDNA band of the expected size (~600bp); in fact, it is disappearing upon complete fragmentation of the insert. As a radiation source, the 60Co-charged device 'Issledovatel' (PNPI) was in use. The tubes with a crude bacterial lysate containing the target (vector with an insert in a cell debris mix) were put at the bottom of a stain steel thermos (with the help of heavy load) filled with the liquid nitrogen. The dose rate was 5kGy per hour. The down-up of the irradiation camera was taken 18Gy only. The time series were up to 300kGy (60 hrs). The detection level of the DNA signal in a gel stained with SYNR Gold was about 10pg.

Results. At the ambient temperature, the insert entirely disappeared (DNA stained with SYBR Gold) upon the doze ~7.5kGy while under the deep freeze at -195.8oC – ~270kGy what accounts for ~35 difference. A similar effect was observed at a bit high temperature (-78.5oC – dry ice) (the work in progress).

Discussion and conclusion. Such a considerable difference in dsDNA 'survival' may benefit in resisting DNA (microbial) to radiation damage and help in searching freshly deposited from the below (ice crust) extraterrestrial life on icy moons and planets despite their harsh radiation conditions at the surface. It seems there is a chance to pick freshly flushed out microbes/DNA on the Jovian Europa (via tidally driven ice sheet cracks) to verify the extraterrestrial life.

STUDY OF AUTONOMIC REGULATION OF CIRCULATION IN CONDITIONS OF PROLONGED ISOLATION

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The dynamics of adaptive reserves and the functional state of the cardiovascular system in conditions of prolonged isolation have been analyzed in 6 crew members (3 men, 3 women). The crew members performed daily self-monitoring of their conditions in the morning hours using a wireless device for ECG registration with data transmission via Bluetooth and receiving results in the online mode. The data of subjective sleep quality self-assessment, blood pressure measurements and heart rate variability (HRV) analysis were evaluated. 682 examinations were carried out including pre- and post-confinement period.

In conditions of prolonged isolation, almost all crew members have experienced fluctuations in the functional state from normal to prenosological and even, in any cases, premorbid. Analysis of the obtained data about autonomic regulation of the circulatory system and HRV under conditions of 120-day isolation has shown that in this experimental group the conditions with a shift in the autonomic balance towards the activation of the parasympathetic gain prevail. At the same time, the analysis of blood pressure and heart rate data indicates a high level of expended energy, providing linear and volumetric blood flow velocity necessary for the proper oxygen supply to tissues at rest and during physical activity.

The individual and gender characteristics of the heart rate and circulatory system regulatory mechanisms consistency were revealed, the stages of adaptation to the conditions of 120-day isolation were highlighted. The obtained results made it possible to formulate both a general model of changes in heart rate variability under conditions of 120-day isolation, and individual models based on the analysis of individual monitoring data. Subsequent research should provide additional evidence to support or refute these models. The results of the experiment with 120-day isolation suggest the need to apply methods of personalizing monitoring results in future projects for a more accurate assessment of the functional state of the crew members.

STANDARD MEASURES DURING SPACEFLIGHT

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The key goal of the *Spaceflight Standard Measures* project is to ensure that a set of measures, representing the Human Research Program's key risks and acquired with minimal impact on time and resources, is consistently captured from crewmembers through the end of the International Space Station (ISS) Program.

Data collected under the *Spaceflight Standard Measures* project include assessments of sleep/wake cycles, cognition, immune status and function, general blood and urine chemistry (urine is collected only before flight and after landing), microbiome composition (gastrointestinal tract, saliva, and body surface), cardiovascular structure and function (carotid intima-media thickness, orthostatic responses), sensorimotor function, and team processes. Data is collected once or twice before the flight (180 and 90 days before launch), twice during the 6-month missions (close to flight day 30, and 30 days before return to Earth) with the exception of actigraphy, which is recorded during two-week periods before, during, and after the mission.

In this presentation, we will review the data collected to date on eight ISS crew members. These data are placed in the NASA Life Sciences Data Archive and are available for occupational surveillance (using non-identifiable data) Institutional Review Board-approved data sharing requests, and retrospective data requests. This data repository enables high-level monitoring of the effectiveness of countermeasures and meaningful interpretation of health and performance outcomes for various mission durations. The knowledge gained from this project informs and supports future hypothesis-driven research that will enable the success of planetary missions.

REVIEW OF SPACE RADIATION HEALTH RISKS FOR EXPLORATION MISSIONS

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Exploration mission safety assurance requires the understanding of space radiation risks and limiting risks to acceptable levels. We describe areas where accurate risk estimates occur and open areas where future research should be the focus. Predicting the health risks from galactic cosmic ray (GCR) exposures to humans carries large uncertainties due to the qualitatively distinct microscopic energy deposition and early biochemistry of heavy ions compared to low linear energy transfer (LET) radiation, such as X-ray or gamma-rays. Radiobiology research on heavy ion effects is essential to develop accurate risk projections and understand the need or approaches to mitigations.

Animal studies of solid cancer risk estimates for GCR suggest fatal cancer risks for long-term space missions could approach 20% fatality with shorter latency than cancers from low LET radiation. This high efficiency of heavy ions in causing solid cancers has several components. First the initial DNA damage is more complex than low LET radiation, including a large relative biological effectiveness (RBE) for gene mutation and chromosomal rearrangements. Second high LET radiation, such as heavy ions and low energy protons and helium ions, are shown to cause non-targeted effects (NTE), which dramatically increase risks at low dose where not all target cells are traversed by ions. The quality of heavy ion tumors is also distinct with more aggressive tumors, shorter latency, and decrease immune cell infiltration into tumor volumes. This later aspect is a more recent observation and suggests a possible role for synergistic risks from space radiation and immune changes due to microgravity.

Space radiation risks for non-cancer effects are diverse in nature. The risk of acute radiation syndromes from solar particle events is readily avoided using passive shielding and alert dosimetry. The risks of circulatory diseases are shown to be small but perhaps non-zero. A larger concern is a significant probability of vision impairing cataracts with short latency (<3 years) and cognitive and memory detriments during a mission. We review results from heavy ion accelerator-based animal experiments with heavy ions on cognition to a Mars mission exposure that would suggests only a small risk. However, microgravity effects and other spaceflight factors could influence cognition suggesting a synergistic detriment. Because of the limitations in mice and rats in representing human brain function and inadequacy of ground-based models of combined stressors, we discuss alternate approaches to gather the necessary information on impaired cognition for the first Mars mission crews.

THE FUNCTIONAL STATE OF THE OPTIC NERVE AFTER A LONG-TERM SPACE FLIGHT

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In the light of solving the problem of the etiology of space neuro ocular syndrome (SANS), a comparative analysis of the functional and morphometric characteristics of the optic nerve of astronauts after a long space flight has been carried out.

Analysis of the computed tomography results of the optic disk on the first day after the flight shows signs SANS risk, namely, its symptom - morphometric changes in the optic disc. Sectoral thickening of the neuroglia was recorded in 80 % of cases by the first day of the flight. By the 14th post-flight day, the state of the optic nerve disk according to the OCT data was comparable to the background, pre-flight.

The functional state of the visual system was assessed by the method of spatial contrast sensitivity (SPR). By the first and 7th post-flight days, changes in PSN were noted. In 30 % of cases, a decrease in sensitivity was recorded in the range of medium and low spatial frequencies, which may indicate a decrease in the activity of the optic nerve magno system, which formed by specific retinal ganglia cells. (Kulikovsky, Robson, 1999; Gouras, 1968; Kaplan and Snapley, 1986; Kulikowski, 1987; Lee, 1990; Livingston, Hubel, 1988). By the 14th day after the flight, the PFC values were comparable to the background values. The state of activity of the magno and parvo- channels of the optic nerve conduction system may be additional important characteristics of the SANS syndrome.

PARASYMPATHETIC REGULATION OF HEMODYNAMICS IN HEALTHY MEN UNDER HYPOMAGNETIC CONDITIONS

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Introduction. To solve the promising problems of space physiology and medicine, studies that simulate the long-term impact of hypomagnetic conditions (HMC) on the activity of the physiological systems of the body, including the cardiorespiratory and autonomic nervous systems, are relevant, since hypomagnetic conditions will occur during interplanetary flights or when people are on the Moon. The long-term effect of HMC on the body of practically healthy people remains poorly studied. In the available sources, we could not find data on changes in the parameters of central hemodynamics (heart rate (HR), blood pressure (BP)) and the autonomic Kerdo index (AKI) under the long-term effect of the HMC factor.

The aim of the study: to search for patterns in changes in central hemodynamic parameters: heart rate, blood pressure (for each cardiac cycle), AKI and blood oxygenation in artificially created HMC.

Material and methods of research. In experimental hypomagnetic conditions, the study of hemodynamics was carried out in 8 practically healthy men who were at rest and in a sitting position. HMC were created on a hypomagnetic stand using the «Arfa» device (result of intellectual activity No. 684-871-913 of 09.09.2019), which reduces the magnetic field induction by more than 800 times, the magnetic field induction inside the device when simulating the HMC was 0.044±0.008 μT, while without the HMC, the magnetic field induction inside the chamber was 44.32 ± 0.32 μT. ECG, heart rate, blood pressure, and SpO2 were monitored using an autonomous portable device SOMNOtouch NIBP (SomnoMedics, Germany), followed by the calculation of the AKI for each cardiac cycle, for 8 hours in two series of observations - under the action of the Earth's natural magnetic field and with HMC.

Results. After a comparative analysis of the measurement results, significant changes in hemodynamic parameters in the HMC have obtained in comparison with the control studies. The heart rate in most cases decreased by an average of 4 beats per minute. Blood pressure in the vast majority of cases significantly decreased: diastolic blood pressure (DBP) – on average by 11 mm Hg, systolic blood pressure (SBP) – on average by 16 mm Hg, which led to an increase in the AKI in the HMC, which increased by an average of 20 % (in 6 cases out of 8). The saturation of blood hemoglobin with oxygen under the influence of HMC have not changed. The polynomial models of the AKI during the time of exposure to HMC are found.

Conclusion. For the first time, for a long time (within 8 hours), the effects of HMC on the regulation of the cardiovascular system in practically healthy volunteers who were in a state of wakefulness and relative rest in a sitting position have been researched. A physiological interpretation of the results is proposed: HMC at rest and in a sitting position in most cases have caused a significant decrease in the modulating effect of the parasympathetic autonomic nervous system on cardiovascular activity compared to control studies conducted under the same conditions, but without the HMC factor.

EXPOSURE OF MICROORGANISMS IN OUTER SPACE

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Biological experiments carried out at space stations over the past decades indicate that the survival of microorganisms in space depends on multilayerness of the exposed samples, the degree of protection of biological objects from UV radiation and

vacuum, as well as on the speed of their transition to a low metabolic state. In order to address the issue of the survival of microorganisms in open near-Earth space, exposed to the harmful effects of various physical factors, such as vacuum, solar radiation, ionizing galactic radiation, etc., a number of countries have conducted experiments on space stations. They show, in particular, that bacteria and mold fungi are able to survive for 31 months. In all experiments, there was a barrier between the microorganisms and the effects of all open space factors, reducing the impact of space. The exposition of open biological objects was carried out in our space experiment «Test».

In the «Test» experiment, cultures of bacteria, archaea, and micromycetes were applied to the surface of sterile cotton swabs. For 2 years, these cultures were exposed on external surface of the ISS without protection from UV radiation, vacuum and other factors of space. Several devices carry viable microorganisms: spores of *Bacillus pumilus*, fungi *Aureobasidium pullulans*, and archae *Methanosarcina mazei*.

The analysis of the results of exposure made it possible to assess the dynamics of maintaining the viability of microorganisms in open space. Trends in the decrease in the number of bacteria and fungi have been revealed: for the first year, the number of CFU (colony-forming units) decreased by 3 orders of magnitude; for the second year, the number of CFU decreased by 2 orders of magnitude compared to the first year. After 2 years, different cultures showed the same decrease in the number of the studied microorganisms. Comparative analysis of microbial genome fragments before and after exposure in open space showed no significant changes. The high surviving rate of exposed microorganisms proves their resistance to the space environment. As such, these microorganisms are able to withstand hard cosmic radiation.

GRAVITY FACTOR IN DETERMINATION OF HEMODYNAMICS REGULATORY SETTING IN HUMAN

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The purpose of this study was to show the dynamics of the ratio of arterial hypo- and hypercirculation in postanal ontogenesis.

Material and methods. The observation group consisted of 1,944 people (1,308 men and 636 women). Patients with acute conditions and exacerbations of chronic diseases were excluded from the examination. The samples are presented in tables and were formed in accordance with the classification of stages of ontogenetic adaptation to the Earth's gravity in the process of formation and life activity in typical human conditions of upright walking. The study was carried out with program and apparatus device «ANTHROPOS-CAVASCREEN» (Ukraine – Poland) is basing on rheography standing and after 15-20 minutes in standing and lying (supine) positions. When going beyond the lower limit of the AP indicator, a decrease in arterial blood flow and arterial circulatory insufficiency syndrome (AC2) are identified, and an in case of beyond the upper limit of this parameters is fixed an increase in blood flow and arterial hypercirculation syndrome (AC1). Each of the age samples can be represented by AC1 and AC2. Hence, the group characteristic of arterial circulation is estimated by the ratio (% of the sample) of opposite-directed syndromes (AC1 / AC2) by blood circulation units.

Results. Outside of the active «anti-gravity» stress of the circulatory state of the cardiovascular system (CVS) in the supine position along the arterial circulation (AC1/AC2) during the pre-definitive stage of postnatal ontogenesis and during the period of the greatest stabilization of the circulatory state, the CVS at the age of 22–35 years is characterized by an adaptive state in which hypercirculatory syndromes prevail in both men and women. At the same time, for the vast majority of AD cells, there were no circulatory insufficiency syndromes (AC2) for the designated age period out of 40 positions for 35 ($P < 0.01$) or their manifestation was low. Starting from the 2nd reproductive age (older than 35 years), a permanent increase in the absolute value of the proportion of syndromes is detected circulatory insufficiency in arterial blood flow, which reflects the systemic nature of age-related changes. Both men and women showed transient and adaptive maladaptive states. Age-related changes in transient and disadaptive states before and after 35 were statistically significant ($P < 0.01$). Basically, these changes were localized in the regions of the pelvis-hip and lower leg (in total, men and women in 9 cells out of 12, $P < 0.05$).

In the standing position, the ratio of AC1/AC2 syndromes in arterial circulation changes significantly due to the regulation of blood circulation by the gravitational (hydrostatic) factor. Regardless of gender (in men and women) and almost throughout postnatal ontogenesis, dysadaptive states are reliably detected by the prevalence of circulatory insufficiency syndromes (AC2) in the blood circulation of the pelvis and lower extremities (red matrix cells, in men and women 12 out of 14, $P < 0.05$). While the age dynamics was similar to the lying position in the abdomen and blocks located at or above the heart (lungs and head). It was in these departments that the age component was manifested, although less pronounced in comparison with the supine position, which in samples older than 35 years, especially in women, was reflected by an increase in with a parity ratio of circulatory syndromes of adaptive orientation (AC1) and circulatory insufficiency (AC2).

Conclusion. The ratio of opposite hemodynamic phenomena, such as circulatory insufficiency in arterial blood circulation and adaptive arterial hypercirculation, reflects the direction of the regulatory setting of the circulatory state of the cardiovascular system. In standing position prevails «anti-gravity stress», which eliminates the age component detected in the supine

position. In the supine position, under the conditions of minimal impact of the gravitational factor, adaptive conditions prevail up to 35 years. After 35 years the transition and disadaptive states were registered rottenly. Changes are mainly detected in the standing position in the pelvis-hip and leg block, and after 35 years are fixed in the lying position.

RADIATION DOSE ASSESSMENT THROUGHOUT THE SOLAR SYSTEM

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Space radiation is a significant risk factor for humanity. Radiation acts in the atmosphere, on the low-Earth orbit, during interplanetary flights, on and beneath the other planets' surface. Radiation dose assessment with numeric methods fulfills gaps of the experimental measurements, allowing extrapolation of missing data to get the comprehensive coverage. Numeric methods allow predicting radiation dose that is very important for decision making and mission planning. They also allow for tracking radiation doses in the past and getting information for the planet's surface and atmosphere evolution.

With the current paper, we give a general overview of our activities, the methods we used and the results we obtained during the last years. We present the radiation dose assessment results for the aircraft altitudes and its dependence geographical coordinates, altitudes, and on the shielding. We describe our efforts to model the ISS's radiation environment and verify the results with the experimental measurements. We discuss radiation dose rates during interplanetary flight and provide our assessment of the optimal shielding, flight time, and maximal mission duration. We address the question of radiation doses on and beneath the planets' surface in the context of the nearest plans of different space agencies.

PAST, PRESENT, FUTURE OF EXERCISE AND HUMAN PERFORMANCE IN SPACE

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Background. Long duration spaceflight results in deconditioning of neuromuscular, musculoskeletal, and cardiorespiratory systems leading to a decline in performance capabilities. Exercise countermeasures have been the primary non-pharmacological means of mitigating degradation in human physiology and performance capabilities during spaceflight. Technological advances in exercise systems and increased knowledge in how to prescribe exercise in flight has led to improved, but not full protection in these physiological systems during ISS missions. Expanding human exploration and habitation beyond low earth orbit will require crew to perform more physically and cognitively demanding mission tasks compared to ISS design reference missions, with increased autonomy. Accordingly, countermeasures will need to be at least as effective as ISS systems, which will be a technological challenge given the limited volume and upmass capabilities associated with exploration vehicles. Failure to maintain crew health and performance could result in loss of mission objectives and well as increase the risk for crew injury or even loss of life.

Purpose. The primary goal of this presentation is to inform the audience on the current state of knowledge on exercise countermeasures systems and the physical requirements that need to be protected for performing mission critical ISS and exploration tasks. Areas that will be specifically covered include: 1) Pre-ISS and ISS exercise countermeasures and measured effectiveness; 2) A timely update on current ISS exercise countermeasures hardware and software capabilities targeted for transition to exploration; 3) Current roadmap for exploration exercise countermeasures systems.

FOUNDERS OF BIOMEDICAL TRAINING OF MANNED SPACE FLIGHTS

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In the Soviet Union, the study of biomedical problems of stratospheric flight was entrusted to the Science Research and Test Institute of Aviation Medicine. A team of researchers led by V.I. Yazdovsky was formed to conduct biological experiments with animals during rocket flights. The life sciences program included the study of the possibility of flying at the cosmic heights

of living organisms in an airtight cockpit. In 1948, V.I. Yazdovsky became the head of the laboratory of biomedical research in order to develop life support systems for spacecraft. On July 22, 1951, the world's first successful launch to an altitude of 100 km of geophysical rocket, in the airtight cockpit of which were dogs Desik and Tsygan. Upon reaching an altitude of 100 km, the animal compartment separated and a parachute opened at an altitude of 7 km, ensuring their safe landing. Thanks to this experiment, it was proved that living organisms could stay safely at cosmic heights. For the physiology and hygienic training of such flights, the staff of the Institute A.V. Pokrovsky, V.I. Yazdovsky, A.D. Seryapin and V.I. Popov were awarded the Stalin Prize. In 1956, in the Institute under the leadership of V.I. Yazdovsky created a department of research and medical support for flights to the upper atmosphere. Senior scientists O.G. Gazenko, A.M. Genin, I.S. Balakhovsky, E.M. Yuganov, A.D. Seryapin and B.G. Buylov studied the possibilities of active animal survival in airtight compartments of rockets during long flights in the upper atmosphere. Installations were created for the long stay of animals for 15 days in airtight conditions with automatic devices for feeding and registration of physiological functions and hygiene parameters. In 1957-1958, 11 rocket launches were carried out at altitudes of up to 212 km and 3 launches at altitudes of 450–473 km. This became a stage of biological sensing of future routes of space flights and a test of the reliability of all systems of spacecraft. V.I. Yazdovsky and his staff were directly engaged in the biomedical preparation of human space flight and ensuring the safety of his return to Earth. Orbital flight of the spacecraft with Belka and Strelka lasting more than a day showed that staying in weightlessness and overload braking during the descent of the spacecraft to Earth, as well as space radiation did not pose a threat to the lives of animals. The safe return of the animals to Earth was a harbinger of human spaceflight and the basis for subsequent tests of the spacesuit, personal protective equipment, life support systems and landing with the help of a catapult chair and in the ship itself. The next flight on the satellite spacecraft on December 1, 1960 went dog Pcholka and Mushka, followed by the flight of the dog Chernushka on March 9, 1961 and the dog Zvezdochka on March 25, 1961. These missions actually completed a period of «biological indication of human spaceflight». They served as the basis for the final decision on the possibility of human flight on the Vostok spacecraft.

ELECTROMAGNETIC COMPATIBILITY OF CARDIOVASCULAR AND RESPIRATORY BIOMEDICAL EQUIPMENT IN GROUND BASED STUDIES OF HUMAN SPACE EXPLORATION

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Ground based simulation studies of human space exploration become more and more international and complex involving many devices produced in different countries with different regulations. Many of these devices transfer data by Wi-Fi, Bluetooth and other wireless protocols. Electromagnetic compatibility (EMC) of experimental devices becomes crucial for success of studies and should be considered during planning of studies. Here we consider the main problems of such planning on the example of cardiovascular and respiratory biomedical equipment, because corruption of data of ECG, pulsoxymeters, blood pressure monitors is one of important consequences of EMC violation.

To prevent any disturbances in the medical equipment functions, the International Electrotechnical Commission (IEC) published the new 4-th edition of the IEC 60601-1-2 standard with special attention to EMC and electromagnetic interferences.

In this standard for the first time, they gave of three exploration environments: professional medical facilities, medical devices in homes and special environments. This subdivision implies differences in equipment usage and electromagnetic environment.

The USA, Canada and EU in 2021 adopted the 4-th edition of IEC 60601-1-2 standard. Foreign producers of biomedical equipment for these countries follows the standard as well. However, some other countries did not adopt the 4-th edition of IEC 60601-1-2 standard.

In March 2015 the 3-th edition of the IEC 60601-1-2:2007 standard was adopted in Russia as State Standard (GOST) R IEC 60601-1-2-2014. According to the 4-th edition of IEC 60601-1-2 standard, the tested equipment tolerates radio emission of up to 28 V/mV. Nevertheless, in the Russian equipment there is no such demand according to State Standard (GOST) R IEC 60601-1-2-2014.

Therefore, the Russian equipment could be non-compatible with the current IEC requirements concerning EMC.

Conclusion. One should pay special attention to electromagnetic compatibility of biomedical equipment including country and year of production as well as electromagnetic environment when planning complex ground based international studies of human space exploration. It seems reasonable to use biomedical equipment produced under the same 4-th edition of IEC 60601-1-2 standard, including Russian equipment produced for export to USA, Canada and EU.

MICROECOLOGY OF THE FUNCTIONAL CARGO BLOCK (FGB) UNDER CONDITIONS OF LONG-TERM OPERATION

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Introduction. During the operation of a space habitable object, the microbiological safety of the environment of the inhabiting crew members plays an important role. In 1998, the Functional Cargo Block (FGB) was put into operation and is currently operating. Over the long period of work of the FGB, exceeding of the normative indicator for the content of bacterial and fungal microflora on the surfaces of the interior and equipment, in the panel spaces, on the structures of the product, and also in its gaseous environment was revealed. In connection with the long-term operation of the FGB, technical and medical risks arise caused by the growth and development of microorganisms in the internal volumes of the product, which requires more careful control, both by specialists-microbiologists and designers operating the facility.

The aim of the work was a comprehensive assessment of the state of the FGB during its long-term operation.

Materials and methods. During the operation of the module, air samples are regularly taken from certain surfaces of the interior and equipment, including spaces behind panels and product structures, which are of particular interest as the conditions of increased contamination, for example, panel spaces with poor ventilation, due to the possibility of a special community of microorganisms – biodestructors forming in these zones. Registration of the microstate of product surfaces in potentially dangerous zones of microdestruction development using digital technologies to form a database of digital images of surface fragments with signs of microdestruction (spots, discoloration, ulcers, colonies of microorganisms).

Results and discussion. To date, more than 200 species of various bacteria and microscopic fungi have been found in space objects, including microbes – technophiles - biodestructors and pathogens of biocorrosion. The evolution of microflora in these conditions is accompanied by the emergence of risks that can have a negative impact, both on the sanitary and microbiological situation, and on the safety and reliability characteristics of space technology. During the monitoring period, the processes of biodamage and biocorrosion of interior structural materials, equipment and structures of the FGB, the appearance of failures and disruptions in the operation of individual links of regenerative life support systems were determined. In the process of work, it became possible to determine potentially dangerous zones for the development of microdestruction using special equipment, and identify zones with environmental parameters favorable for the development of microflora (stagnant zones, zones with high humidity and temperature on the surface close to the dew point, increased levels of the ultrasonic range, etc.).

Conclusion. Systematic monitoring of the internal environment and structures of the module made it possible to see the complete picture of the microbiological state of the FCB, develop measures to stop the processes of biodegradation and disruption of equipment performance, and improve the internal environment of the crew members. The data obtained on the evolution of the microbial community can also be taken as a basis for the creation of medical and technical requirements, developed for the purpose of the implementation of a manned lunar expedition and the functioning of the inhabited lunar module.

SPACE RADIATION AND CENTRAL NERVOUS SYSTEM IMPACTS: NASA STANDARDS AND EVIDENCE

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It is well understood that large radiation localized doses to the brain cause clinically significant impacts to the central nervous system in human populations. However, the effects in adults exposed to lower doses remain unclear due to lack of data in relevant human cohorts. The impact of exposure to high-energy particles is even less understood. NASA's Human Research Program relies heavily on model systems to characterize the impacts of the space radiation environment on the human brain and how potential changes may effect mission success and long term health and well-being. Animal, cellular, and molecular experiments implicate multiple – and possibly related – mechanisms that mediate impacts to the central nervous system in model systems including, but not limited to inflammation, immune responses, oxidative stress, metabolism, myelination, molecule transport, electrophysiology, and a variety of "omic" changes. While animal studies demonstrate potential changes across a number of cognitive and behavioral domains the direct applicability to the astronaut population remains unclear. Furthermore data access experiments and model systems can be inconsistent and dependent on multiple experimental variables indicating a clear need for robust validation. To minimize potential impacts to astronauts NASA limits dose to the CNS based on a combination of terrestrial epidemiology informed by experimental evidence in model systems. To date no recommendations have been provided by the National Committee on Radiation Protection and Measurements. This presentation will provide an overview of NASA's current dose limits for CNS exposure to space radiation as well as highlights of the current state of evidence and ongoing research.

BRAIN STEM CELLS, NEW NEURONS, AND RADIATION

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Manned exploration of space is accompanied by increased exposure to various types of radiation. There is emerging realization that among the risks associated with spaceflights are the effects that radiation may exert on the cognitive and emotional status of the explorers. These effects are mediated, in part, by the damage that radiation inflicts on neural stem cells and newly generated neurons of the adult brain. Newborn neurons that are produced in the adult hippocampus are involved in learning and memory, emotional state, and response to stress. Dividing stem and progenitor cells of the hippocampus are highly vulnerable to radiation, and various types of radiation exposure, e.g., during cancer therapy, effectively disrupt neurogenesis and production of new hippocampal neurons. Notably, this disruption is thought to underlie some of the impairments that with high incidence accompany radiation therapy, such as deficits in short- and long-term memory and learning, as well as increased anxiety and depression. Similar considerations pertain to spaceflights beyond low Earth orbit; therefore, understanding the basic mechanisms and consequences of radiation-induced damage to adult hippocampal neurogenesis is critical when considering the strategies for preventing or mitigating the neuropsychological effects of the deep space radiation exposure.

We study the effects of irradiation on adult hippocampal neurogenesis in animal models and humans. Our results reveal distinct changes that various types of radiation inflict on dividing neural progenitors and their immediate progeny. Unexpectedly, we found that quiescent neural stem cells, expected to be more resistant to the effects of radiation, show even higher sensitivity to radiation than their rapidly dividing progeny. Our results also demonstrate the delayed effects that exposure to radiation has on the cognitive reserve and complex features of learning and memory, such as pattern separation and re-learning. We will discuss the results in the context of differential susceptibility that radiation may have on distinct steps of the division and differentiation cascade of neural stem cells in the adult brain and on the associated cognitive function.

GRAVITY-DEPENDENT CHANGES IN THE FUNCTIONAL STATE OF THE NEUROMOTOR APPARATUS OF THE RAT CALF MUSCLES

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The study of the processes of reorganization of the motor function in the conditions of a changing gravitational environment is an urgent task of neurobiology and medicine.

On laboratory rats weighing 190–210 g, in compliance with all bioethical standards, the functional state of the neuromotor apparatus of the calf muscles was studied under conditions of simulated hypogravitation, as well as posthypogravitational readaptation. The method of antiorthostatic hanging (Ilyin E.A., Novikov V.E., 1980; Morey-Holton E.R. et al., 2002) in animals (n = 15) simulated of the hind limbs gravitational unloading (HU) for 35 days. After HU, as well as on days 1, 3, 7, and 14 of readaptation, the functional state of the following neuromotor systems was assessed: m. soleus (SM), m. tibialis anterior (TM) – the corresponding spinal motor centers. The motor and reflex responses of the muscles were recorded and analyzed. A decrement-test of the M-response was performed with repetitive stimulation of the sciatic nerve (3 Hz, 50 Hz). The data obtained in the study of intact animals (n = 7) were used as controls.

The results of assessing the parameters of the H-response after HU indicated an increase in the reflex excitability of the SM and TM motor centers ($p < 0.05$). However, already on day 1 of readaptation, a decrease in reflex excitability of the corresponding motor centers ($p < 0.05$). On day 3 of the readaptation period, an increase in the amplitude of the SM H-response ($p < 0.05$) and the H/M ratio ($p < 0.05$) was found. In addition, it was found that at all studied stages of readaptation, the duration of the SM H-response increased and, on average, was 126 ± 7 % ($p < 0.05$). When evaluating the parameters of the SM M-response, it was found that after 35 days of HU, the threshold of the M-response was 75 ± 13 % ($p < 0.05$); on day 1 of readaptation, the threshold of the M response increased to 156 ± 11 % ($p < 0.05$); maximum amplitude of the SM M-response after 35 days HU was 73 ± 11 % ($p < 0.05$), on day 1 of readaptation – 68 ± 13 % ($p < 0.05$), on day 3 of the readaptation period the amplitude increased to 128 ± 12 % ($p < 0.05$). Also, during the period of readaptation, an increase in the duration of the SM M-response, on average, up to 118 ± 6 % ($p < 0.05$). When testing TA, an increase in the M-response threshold to 121 ± 8 % ($p < 0.05$) was recorded on day 1 of readaptation. The results of the decrement-test (50 Hz) SM and TA M-response both after HU and during readaptation showed a significant decrease in the reliability of neuromuscular transmission.

Thus, under conditions of limitation and subsequent restoration of the action of the reaction force of support and axial loads and, as a consequence, changes in the intensity of peripheral afferentation, first of all, support afferentation, there is a change in the functional state of the motor centers and the peripheral structures of neuromotor systems under their control. The processes of gravitational-dependent motor reorganization are more pronounced in the tonic «anti-gravity» muscles.

The reported study was funded by RFBR according to the research project No. 19-04-01067.

WHOLE-BODY VIBRATION: AN 18 MONTH COUNTERMEASURE EVALUATION OF POSTMENOPAUSAL WOMEN

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Introduction. Osteoporosis exhibits a profound reduction in bone mineral density (BMD) with significant microarchitectural alterations$_{(1)}$, widely evidenced as a debilitating condition with significantly higher instances of osteoporotic complications in post-menopausal women$_{(2)}$. While the issue of bone loss in women remains terrestrial, similar BMD findings are common, following prolonged exposure to microgravity$_{(3)}$. Current treatment relies on pharmaceutical and exercise intervention, which have yielded some positive effect$_{(4-5)}$. Several studies have investigated the osteogenic effect of whole-body vibration (WBV)$_{(6-7)}$, however, due to numerous frequency variations (high/low), different magnitudes (<1g/>1g) and exposure intervals to the vibration stimuli, uncertainty remains. To ascertain WBV efficacy, osteogenic effect on post-menopausal women was scrutinised using high-frequency vibration with a combination of high and low-magnitude stimuli. The primary focus was to discern femoral neck changes, while also evaluating bone microarchitectural differences and observing whether the osteogenic effect of WBV remained post-vibration protocol, an experimental combination previously unreported.

Methods. Postmenopausal women (100 control;100 treatment group) aged 55–75yrs participated in this study. The initial 12-months consisted of the vibration protocol (vibration group) and regular visits (control group), then a 6-month follow-up period for both groups. Participants without adverse medical conditions and FRAX index (5–35 %) were selected.

During each 20-minute session (3-sessions/week, 130 sessions total) light squatting and stretching exercises were performed. The first session was shorter and interspersed with rest periods. The vibration characteristics during all exercise protocols were: frequency (30–50 Hz), acceleration (0.75–7.04 g) and a combination of low-amplitude (0.2-0.4 mm) and high-amplitude (0.6-0.8 mm) stimuli was delivered using PowerPlatePro5 air adaptive-system (Performance Health Systems, LLC, North Brook, IL, USA). This system was selected for its tri-axial accelerations (X, Y, Z axis) and self-adjusting air cushion system that controlled for participants weight distribution across the platform, mitigating against dampening.

Measurements were taken at baseline, month 6, 12 and 18. Both groups presented to the rheumatology department for fasting sample measurements of C-terminal crosslinked telopeptide of type-1 collagen (sCTX), procollagen type-1 N-terminal propeptide (P1NP), bone alkaline phosphatase (bAP) and sclerostin (SOST). Subsequently, anthropometric and densitometry parameters (BMD of the whole-body, femoral neck, lumbar vertebrae and superior aspect of the femur (excluding the femoral neck) were measured using dual-energy X-ray absorptiometry (DEXA). Finally, bone microarchitecture using high resolution peripheral QCT(HRpQCT) (Xtreme CT, Scanco Medical, Bassersdorf, Switzerland) of the non-dominant radius and tibia was performed. Statistical analysis was performed using a generalised mixed-linear model with age as a covariate. The results were reported as mean±SE and significance level set at ($p = 0.05$).

Results. Preliminary DEXA results for the vibration phase, indicated a progressive reduction in lean body mass ($p = 0.042$) in the vibration group (37326.17 ± 440.32g) compared to control (38599.12 ± 492.63g). Total body mass between control (68126.80 ± 1513.91g) and vibration (64444.23 ± 1104.81g) also decreased($p=0.020$) when comparing baseline and month 12 ($p = 0.020$). Despite fat mass demonstrating a similar trend, no significant change was observed ($p = 0.067$). No other changes for DEXA, biological markers and HRpQCT parameters were detected.

Conclusions. Despite integrating high frequency and acceleration profiles with varying magnitudes, throughout all exercise protocols, the effects on bone and its microarchitecture appear unaltered. However, changes to lean body mass are likely to be observed. These results also emphasize the need to investigate direct local vibration exposure to osteoporotic specific zones.

EXAMINING TEAMWORK OF SPACE CREWMEMBERS AND MISSION CONTROL PERSONNEL UNDER CREW AUTONOMY: A MULTITEAM SYSTEM PERSPECTIVE

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Introducing crew autonomy into the design of future space operations will involve a change in how responsibilities are going to be distributed between crew and mission control and may disrupt the functioning of the space/ground multiteam system (MTS). The present study is the first of a series of studies exploring the impact of crew autonomy on the functioning of the space/ground multiteam system.

Method: During a 4-month space mission simulation we collected survey data from 6 crewmembers (4 Russians – 3 female and 1 male; 2 US – both male) and 24 mission controllers tapping their team concept, perception of cohesion among members of the space/ground multiteam system, as well as their assessment of the multiteam system's efficacy, task work and performance.

Results and Discussion: Preliminary analyses indicate differences in crewmembers' and mission controllers' team concepts as both focused on members of their own component teams rather than the space/ground multiteam system. Differences were also apparent in perceptions of multiteam system cohesion, efficacy and task work. Mission controllers perceived higher cohesion – especially higher task cohesion – with crewmembers and were more likely than crewmembers to express high confidence in the efficacy of the multiteam system. While mission controllers and crewmembers expressed comparable levels of satisfaction with task performance, they frequently disagreed on how much each component team contributed to task success. It is important to stress that these findings are preliminary as they are derived from one study in an ongoing project; however, they do point to aspects of team cognition in the space/ground multiteam system that may be negatively affected by crew autonomy and could potentially disrupt space/ground collaboration.

LONGITUDINAL EVALUATION OF CARDIAC FUNCTION AND STRUCTURE IN APOE NULL AND C57BL/6J MICE AFTER GAMMA AND SPACE-TYPE RADIATION EXPOSURE

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The cardiac effects induced by space-type IR, specifically simplified GCR simulation (simGCRsim), are yet to be discovered. We hypothesized that gamma (γ) and simGCRsim IR-induced biological responses are chronic, IR type- and dose-dependent and may increase the relative risk for developing cardiovascular diseases (CVDs) during and after long-duration space missions. To test our hypothesis, 3-month old male C57Bl/6J wild type (WT) mice were irradiated with 137Cs-γ-IR at 100-400 cGy and simGCRsim at 50–150 cGy, 500 MeV/n. We assessed cardiac function by transthoracic echocardiography (ECHO) at 14, 28 days, and 12, 16, 22-months post-IR.

Fourteen days post-IRs there was ~20 % decrease in Fractional Shortening (FS%) and Stroke Volume (SV) reduction in 50 cGy simGCRsim-IR mice. This early change were associated with reduced LV size and dimensions (end diastolc diameter [LVEDd], internal diastolic diameter [LVIDd]), while in γ-IR mice there is ~30 % reduction in LV Posterior Wall Thickness (PWth) in systole. The interventricular Septum (IVS) was not altered at 14 or 28 days post-IR. By 28 days, histological changes included multifocal myofiber disarray with mildly increased variation in myofiber diameter, swollen myocytes, vacuolation in myofibers, mild to moderate sarcoplasmic swelling, and minimal multifocal mineralization of few myofibers within papillary muscles. At 12 months, systolic function was significantly reduced in both IR-types, with an ~15 % and ~20 % decline in LVEF. This was accompanied with ~50 % increase in end systolic volume (ESV) in both IR-groups, suggesting a possibility of late-onset CV hemodynamic changes. Global LV systolic function was impaired in γ-IR mice compared to all groups, with ~40 % reduction in LVEF, which was acompanied with significant increase in SV and ESV (~60 %), LV mass (~50 %), LVED and LVId (~40 %), suggesting compensation for LV volume overloade and significant LV hypertrophy. Compared to non-IR and γ-IR groups at 22 months, there was no alteration in LVEF, however, SV and LV mass were elevated by ~50% in 50 cGy simGCRsim-IR mice which is accompanies with increased ESV, LVEDd, and LVIDd suggesting possible compensation for pressure overload via hypertrophy and development of diastolic dysfunction verses systolic dysfunction is this IR type. Cardiac tissue responses, morphology, structure, and underlying molecular mechanisms are being analyzed.

In summary, a single full-body IR at doses of 100-400 cGy for γ-IR and 50-150 cGy for simGCRsim-IR decreases the global systolic function of the heart in WT mice at 14 and 28 days after exposure. Our lifetime study reveals that at these doses, cardiac function is significantly affected at early 14 and 28-day time points and at 22 months post-IR. Interestingly, WT mice have an intermediate time point (12 months) were impairement in LV function is obsevered. Our data suggests, WT IR-mice may be exhibiting more diastolic dysfunction and compensation as a result of pressure overloaded systems. These findings do not exclude the possibility of increased acute or degenerative CV disease risks at lower doses of space-type IR and/or when combined with other space travel-associated stressors, such as microgravity.

DEVELOPMENT OF THE DESIGN OF A COUNTERMEASURE SYSTEM FOR MOON AND INTERPLANETARY MISSIONS IN GROUND AND SPACE EXPERIMENTS

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Exposure to weightlessness leads to adaptive changes in the gravitational systems of the human body. The success of the extravehicular activity at the surface of Moon and Mars missions largely depends on the effectiveness of the system for countermeasures to negative effects of weightlessness. The purpose of the study of the series of ground-based analog experiments and in the space experiment (SE) «Profilactika-2» was to develop a design of the countermeasure system for lunar and interplanetary missions. Analogous experiments included studies with the isolation of volunteers from 120 to 520 days and experiments with «dry» immersion from 5 to 21 days. The space experiment «Profilaktika-2» was implemented at the ISS flights duration from 138 to 205 days. In the SE and experiments with isolation, the evaluation of physical performance was carried out on the basis of a locomotor test with a stepwise increasing load, was register the parameters of the cardiovascular and respiratory systems, as well as the electromyographic (EMG) activity of the leg muscles. Before and after space flight (SF) (or modeling of its factors), testing of the properties of leg muscles by an isokinetic dynamometer and a walk test with the registration of EMG were used.

The results of model studies with isolation showed that training on a passive-mode treadmill turned out to be 7 times more effective than training on a bicycle ergometer, training on an active treadmill – 5 times, training on a strength simulator – 2 times, and training on a vibrating platform – 1.5 times, the least effective were training with the use of resistance bands. The total assessment was based on the summary results of the MO-3 test, tests on a strength simulator and a bicycle ergometer test. The advantage of locomotor training in interval mode compared to continuous mode has been confirmed. In experiments with «dry» immersion without the use of countermeasure means, a significant decrease in the strength of the leg muscles and in the functional reserves of the cardiovascular system were observed. The depth of the changes after «dry» immersion was comparable to the changes after long-term SF. In an SF, it was shown that replacing training on a treadmill by training with a compensator of support unloading or a bicycle ergometer for three days does not lead to significant changes in the response of the cardiovascular system to a test load. During the SF, adaptive changes in the functions of the cardiovascular, respiratory and neuromuscular systems were observed in accordance with the flight stage and countermeasure features. The initial stage of SF for 30 days, accompanied by an increase in the physiological cost of physical activity of all recorded parameters.

Conclusions. The necessity of using countermeasures means in SF duration from 5 to 21 days is shown. The use of passive-mode treadmill is the most effective for the countermeasure of negative effects of weightlessness at the lunar mission.

For an interplanetary mission, it is necessary to expand the set of tools used to prevent monotony, while taking into account the significant differences in the effectiveness of these tools. A support unloading compensator, electromyostimulators and vibration platform can be added to them. Further testing of the effectiveness of new measures in space experiments is required.

The research was supported by basic financing from the Russian Academy of Sciences (63.1) and Roskosmos.

NEUROPLASTICITY AND MICROGRAVITY: GENE EXPRESSION PROFILE CHANGES IN THE MEDIAL VESTIBULAR NUCLEI AND THE INFERIOR OLIVE NUCLEI OF THE BRAIN OF MICE AFTER A 30-DAY SPACE FLIGHT ON THE BION-M SATELLITE

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Gravity is known to be one of the most potent factors that influenced the life from the first forms appearance. It is known that under microgravity conditions, in the absence of an afferent impulses stream, the vestibular control system is one of the first to show changes. Vestibular structures such as the inferior olive nuclei (IO) and medial vestibular nuclei (VE) have been found to be significantly activated in space, but almost nothing is known about the molecular mechanisms that underlie the ability for neuroplasticity in microgravity in these structures.

On May 19, 2013, IO and VE samples were obtained from C57BL6 mice after a 30-day space flight on the BION-M1 satellite. Also, samples from the control group kept for 30 days on Earth under conditions that simulate the habitat on a biosatellite were analyzed. After isolating brain structures, slices were immediately placed in RIPA lysis buffer. The total RNA was isolated and the construction of cDNA libraries was performed according to the TrueSeq protocol (Illumina). Genome-wide gene expression profiling by the RNA-Seq method on the Illumina HiSeq2500 platform was carried out. A total of 14 samples were sequenced (8 space, 6 controls).

Among two vestibular structures, Inferior olives (IO) were shown to be most affected by expression changes, with 224 up-regulated genes and 73 down-regulated (FDR < 0.05). Gene ontology analysis have shown their predominant relation to changes in epithelium («blood vessel development», «epithelial cell differentiation», «hemostasis»; -30, -9 ,-8 Log10(P), respectively), as well as growth factor signaling («response to growth factor», «growth factor binding», -10 Log10(P)). In the last case, transforming-growth factor beta (TGFb) and insulin growth factor 2 (Igf2) signaling pathways were found to be particularly enriched, represented by 4 (Tgfb1, Tgfbr3, Htra3, Lrrc32) and 3 (Igf2, Igfbp2, Igfbp3) up-regulated genes, respectively. In terms of effect size, largest differences were detected in MPZ gene (myelin peripheral protein, ~8 log2FoldChange). Changes in VE, on the other hand, were only significant in 36 genes (11 up-regulated, 25 down-regulated), with 5 up-regulated genes directly related to oxidative phosphorylation/mitochondrial metabolism (ND1, ND4, ND5, CYTB, COX).

Such results indicate that, among two vestibular brain structures, inferior olives could be both especially important for adaptation to space-related gravity changes and/or prone to its stress.

INVESTIGATING NEUROPLASTICITY INDUCED CHANGES DUE TO ARTIFICIAL GRAVITY TRAINING THROUGH CORTICAL FUNCTIONAL CONNECTIVITY & NETWORK ANALYSIS

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Space research has extensively studied the detrimental effects of weightlessness on human physiology. Several countermeasures have been proposed to ameliorate this negative impact of microgravity. Among them, human centrifuge has been a promising tool to maintain a proper cardiovascular and musculoskeletal level during space missions. However, the neuroplasticity effect of artificial gravity training on the brain function remains an open question. The answer of this neuroscientific mystery may improve the countermeasure's efficacy on long term space missions, while it will facilitate the opportunity to transfer this technology from the space sector to the clinical routine in case of patients suffering from neurodegeneration/stroke-related mobility difficulties.

Aiming to shed light into the neuroplasticity effect associated with artificial gravity training, we enrolled 23 (10 female) healthy, young volunteers who performed artificial gravity training in several levels (0.5g, 0.7g, 1.0g, 1.2g, 1.5, 1.7g, 2.0g) as well as standing and lying conditions. Their age was 23.13 ± 3.70 years. Their height was 1.74 ± 0.09 meters, and their Body Mass Index (BMI) level was 24.80 ± 4.67. Neurophysiological data acquisition took place through 19 electrode channels placed to the head surface according to the 10-20 International system. Electrocardiography (ECG), chin electromyography (EMG) and Electrooculography (EOG) took also place. The artificial gravity training was intermittent (5 minutes training followed by 5 minutes of inter-training interval). The analysis involved the reconstruction of cortical activity through sLORETA inverse solution and the estimation of functional connectivity through the synchronization likelihood. Finally, graph theory was used for estimating the cortical network organization. Heart Rate Variability (HRV) analysis was employed to estimate the exercise intensity, while a complete neuropsychological estimation took place in order to assess changes in cognition and functional status.

Preliminary results demonstrated a significant increase in delta and a decrease in beta rhythm during training when compared to the standing condition. This pattern of oscillatory alterations also resulted in a decrease of local information processing (mean cluster coefficient) and a functional disconnection due to diminished information flow (characteristic path length) during the training in comparison with the standing condition. On the other hand, the 1.5g level seems to share greater similarity with the standing condition. This may be an index of optimal training dosage. These results were then used

to investigate whether an intensive (24 sessions & 1 month) rehabilitation program may improve the mobility and functional status of a 54-year-old patient suffering from multiple sclerosis. The results indicated again cortical oscillations and functional connectivity alterations that were similar to the neuroplasticity effect of cognitive and/or physical training programs targeting senior citizens. More importantly, the changes were observed on frontal, temporal and limbic regions, known for being malleable to neuroplasticity interventions.

INCREASING MEDICAL STUDENTS' ACCESSIBILITY TO AEROSPACE MEDICINE WITH AN ONLINE COURSE

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Background/Purpose. To date, there are sparse formal educational opportunities available for medical students to gain more knowledge and exposure to the field of aerospace medicine. The few opportunities that do exist are found at select universities and are in-person experiences, thus limiting their accessibility. As a result, many students around the world remain unaware of the application of and possibilities within this field. A short, online mode of delivery for this content does not currently exist, and this is the gap we aimed to fill by creating a readily adaptable curriculum for an online Aerospace Medicine course.

Methods. The two-week online course consists of ten modules (see full list below) covering topics adapted from the following texts: 1) Fundamentals of Space Medicine by Clement 2) Space Physiology by Buckey and 3) Space Physiology and Medicine by Nicogossian. Each module contains readings, PowerPoint presentations with integrated clinical cases, quizzes, and supplementary assignments (consisting of journal articles, videos, podcasts etc). The course also includes a pre-and post-course assessment and a list of further readings, opportunities, and resources.

Module 1: Introduction and Historical Perspectives
Module 2: Operational and Life Support Systems in Space
Module 3: Preflight and Postflight Recovery
Module 4: Radiation in Space
Module 5: Neuro-Vestibular System in Space
Module 6: Vision in Space
Module 7: Cardiopulmonary System in Space
Module 8: Musculoskeletal System in Space
Module 9: Psychological Considerations in Space
Module 10: Nutrition in Space

Results.The two-week online course was developed over a six-month period by six medical students in the U.S. The pilot iterations of the course launched at the University of Michigan Medical School on Jan 4th, 2021, and there are 18 students currently registered. The qualitative and quantitative data categories that will be gathered include 1) Knowledge Gained 2) Course Satisfaction 3) Course Influence on Future Goals and 4) Quality Improvement/Program Evaluation.

Conclusion. This introductory, online aerospace medicine course will fill a gap in medical education and make the field more accessible to interested students. Our next steps include 1) incorporating students' and subject-matter experts' feedback into the class, 2) piloting the course at other medical schools, and 3) formalizing elective status. Future directions include making the elective widely available to all medical students across the world.

CHANGES IN THE BLOOD PROTEOME OF COSMONAUTS WITH EXTERNAL SIGNS OF MICROVASCULAR INJURY AT THE FIRST DAY AFTER LANDING

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The influence of the overloads of the final stage of long-term space flights (SF) on the human body is an urgent problem of aerospace medicine. The aim of this work was to study the peculiarities of the complex proteomic response of the astronauts' organism associated with the external manifestations of microvascular injury of soft tissues upon landing after prolonged space flights. Blood samples from 13 Russian cosmonauts (mean ± SD age: 44 ± 6 years, all men) were analyzed. According to the results of the examination of the subjects after landing, local petechial hemorrhages in the soft tissues of the back and legs were noted. Proteomic analysis of the samples was carried out by high performance liquid chromatography with tandem mass spectrometry.

For bioinformatics analysis, software packages and information resources Perseus, PubMed, Uniprot, ANDSystem were used. Of the 19 proteins that significantly differed (p-value < 0.05) between the background samples and samples collected at the 1st day after landing, there were nine proteins directly related to vascular injury. It has been shown that among proteins with significantly different concentrations, there are proteins that have a predominantly protective effect from apoptosis of endothelial cells and an increase in vascular permeability, proteins-regulators of the processes of maintaining the rheological properties of blood, proteins-antagonists of the main triggers of postischemic reperfusion damage to parenchymal organs (lungs, liver, etc.). Thus, the complex of proteins with significantly changed blood concentration in cosmonauts with pronounced petechial symptoms gives an idea of the mechanisms and processes occurring in the body expressed at different times. Some of them, occurring during the SF itself, serve as a preparatory stage and make the vascular system vulnerable to traumatic injury. Other processes are activated under the influence of g-forces during landing. Consequently, the measures for arresting (weakening) these negative effects on the vascular system should take into account not only the «locus», but also the application time. The data obtained are the beginning of a new direction of research, which makes it possible to reveal the features of proteomic responses to micro- and macrovascular trauma during overload. Investigation of changes in the blood proteome of cosmonauts in response to micro- and macrovascular trauma during overload on descent after prolonged SF will help to determine the direction of new methods of prevention and, possibly, treatment of injuries, as well as substantiate new approaches and methods to the selection of astronauts. The data presented are of interest to specialists in the field of gravitational physiology, aviation and space medicine.

The work was carried out within the framework of the basic themes of the Russian Academy of Sciences 65.3.

ANALYSIS OF OSTEODENSITOMETRY DATA OF COSMONAUTS AFTER THE FIRST AND REPEATED FLIGHTS CONSIDERING THE TIMING OF THE EXAMINATION AFTER LANDING

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The study of changes in the BMD (BMD) in cosmonauts after space flights is carried out in expert areas of the skeleton by the method of X-ray osteodensitometry in terms as close as possible to the return to Earth: first or second postflight week. Previously, the interpretation of these changes did not consider the possibility of continuing to decrease the BMD after landing, as shown in the work of Vico et al. (2017) when analyzing changes in the mineral density (trabecular and cortical) of the radius and tibia within 3–12 months after landing, as well as the fact that the rate of bone changes can be quite high (Avrunin, 2012). An additional influence on the results obtained can be exerted also by the number of previously completed space flights in the examined cosmonaut (Bonuchi, Silvestrini, 1996; Oganov, 2014; Larina et al., 2018).

The work was aimed to assess the effect on the lumbar vertebrae and the proximal femur BMD of factors such as the week of post-flight densitometry (1st or 2nd one), as well as the repetition of flight, and the combined effect of these two factors.

A retrospective analysis of the BMD of cosmonauts from the Mir orbital station and the International Space Station (flight duration 179 ± 40 days) was carried out. For 47 cosmonauts, a sample of 80 pairs of values (PV; pre-flight and post-flight) was formed. The 1st factor: the 1st group (36 PV) – the first flight, the 2nd group (44 PV) – the repeated flight. The 2nd factor: the first group (43 PV) – measured in the first week after landing, the 2nd group (37 PV) – in the second week after landing.

Data processing was performed by MANOVA with repeated measurements in the Statistica 10 software. Differences were taken as significant at $p < 0.05$. Fisher's test was used to detail the differences between groups.

No statistically significant differences were found between the groups in terms of flight repeatability (1st factor). This confirms the regularity of the individually specific ratio of bone loss in different segments of the skeleton during repeated flights (Oganov et al., 2014).

Statistically significant ($p < 0,05$) differences in the results of measurements of BMD in the first and second week were revealed (2nd factor), while the decrease in BMD in the first week after planting exceeds that in the second. It can suggest that in these areas in the two first weeks after landing the process of bone tissue formation prevails over the process of resorption.

THE SUSCEPTIBILITY OF VOLUNTEER'S T CELLS TO IMMUNOMODULATION DURING LONG-TERM DRY IMMERSION

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Space flight factors such as stress, hypokinesia, microgravity and others adversely affect the immune system. Decreased functional and adaptive activity of immune cells lead to the depletion of reserve capacities, and elevation of inflammatory and allergic reactions (Dhabhar, 2009; Morukov et al., 2011; Rykova et al., 2013).

Multipotent mesenchymal stromal cells (MSCs) are a promising tool for immunomodulation. They have the ability to impact the response of all immune cells, in particular to inhibit the activation and proliferation of stimulated T cells *in vitro* (Rasmusson et al., 2003; Le Blanc et al., 2004; Gornostaeva et al., 2014, 2018). The immune cell susceptibility to MSCs depends on the functional state of organisms.

The aim of this work was to investigate the influence of microgravity simulation in dry immersion (DI) experiments on the susceptibility of T cells to the MSC immunomodulatory impact.

Healthy volunteers (n = 8), men between the ages of 24 and 32, participated in the 21-day DI experiments.

Blood sampling was performed one day before the DI (basal), on the 7th and 21st days of DI, and on the 7th day after DI (rehabilitation). Mononuclear cells from peripheral blood were isolated by density gradient, than T cell ($CD3^+$) isolation by magnetic separation was performed. T cells were stimulated by phytohemagglutinin (PHA) and cocultured with MSCs from human adipose tissue for 72 hours.

After interaction, the T cell late activation as a MHC II antigen expression, proliferation in SbG1 test and the levels of soluble factors in the conditioned medium, were determined.

The MSCs successfully suppressed activation and proliferation, and induced an anti-inflammatory shift of the cytokine profile of T cells collected at basal point.

DI caused an increase in the late activation of T cells and a decrease in their proliferative activity. After DI, the share of activated T cells returned to basal levels, while the ratio of dividing T cells further decreased.

The changes of the T-cell paracrine profiles were subject-dependent. In case of low basal paracrine activity, an inflammatory stimulation under DI and recovery after exit form DI was observed. With high basal level, the suppression of total paracrine activity was detected, recovery did not occur after DI cancelation. T cell paracrine profiles were shifted towards anti-inflammatory upon interaction with MSCs, thus smoothed the effects of DI. Successful suppression of T cell activation and division was observed.

Thus, the dynamics of the response to simulated microgravity depends on the individual features of the subject immune system. The MSCs successfully suppressed immune response of T cells from subjects under DI. MSCs can be used as a supplementary treatment in case of the undesirable inflammatory reactions of cosmonauts in space missions.

The work was supported by Basic Research Program of Institute of Biomedical Problems of RAS, theme 65.3.

DEREGULATION OF COSTAMERE COMPONENTS IN UNLOADING MUSCLE ATROPHY

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Costameres are muscle multiprotein complexes that connect and align the sarcolemma to the underlying sarcomeric myofibrils, coincidently with Z-discs and M-lines, and to the extracellular matrix. Costameres work in a bidirectional manner. They collect forces spreading laterally to the long axis of the sarcomere and channel them across the sarcolemma to the extracellular matrix, by providing up to 70% of the muscle contraction force, and they function as mechanotransducers, transforming mechanical load in biochemical signals, which, in turn, trigger specific responses in term of gene expression, protein synthesis and organization.

Microgravity/unloading not only silences load-dependent costamere signaling, but also induces changes in costamere integrity, affecting the expression and function of several components, both at sarcolemmal and cytoskeletal level. Among these are the neuronal isoform of Nitric Oxide Synthase (nNOS) and the muscle-specific chaperone melusin, which participate in the dystrophin glycoprotein complex and integrin signaling, respectively. Unloading deregulates very early, i.e. before evidence of myofiber atrophy, both nNOS and melusin, after a 6h unloading bout in the rat soleus muscle and 8 days of bed rest in human vastus lateralis.

Neuronal nNOS active molecules quickly disappear from sarcolemma and localize in the myoplasm, while transcripts and total nNOS protein decrease severely, but transiently, during unloading. Use of NOS inhibitors or siRNA showed that the active enzyme is required for nuclear translocation of the FoxO3 transcription factor and atrogene upregulation. Compelling evidence from other laboratories about actual NO levels in unloaded soleus muscle strongly support the possibility that the enzyme activity of the redistributed nNOS molecules implies uncoupling from NO formation. Melusin protein levels decrease early and permanently in the unloaded rat soleus. Expression of exogenous melusin attenuates loss of muscle mass and function, downregulating atrogene transcription, independently from FoxO3 protein levels and activity. In fact, unloading-induced atrophy is fully abolished only when the losses of both active sarcolemmal nNOS molecules and melusin protein are counteracted simultaneously, suggesting that both these events should be switched off to maintain physiological levels of muscle mass and force.

At present, only the unloading-induced nNOS deregulation can be prevented by pharmacological treatments. Among these, the systemic administration of curcumin to unloaded rats for 7 days was effective in decreasing the degree of muscle atrophy

about 30 %. Translatability and effectiveness of a chronic curcumin treatment were addressed recently by investigating mouse sarcopenia. Preliminary results show good tolerance of the administration protocol, absence of toxicity and protection against muscle atrophy development.

LOWER BODY NEGATIVE PRESSURE: CURRENT UPDATES AND PERSPECTIVES

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Lower body negative pressure (LBNP) has been used to investigate systemic compensatory responses during central hypovolemia. There has been a great deal of new research that involves numerous applications of LBNP as a model used to investigate the impacts of human exposure to extreme physiology and medicine. The study of various acute and chronic adaptations to central hypovolemia using LBNP has revealed important interactions between physiological mechanisms with implications for key clinical conditions. This paper examines LBNP from a variety of perspectives, including aspects related to the physiology underlying orthostatic intolerance, blood pressure regulation across the sexes, hemorrhage, and mathematical modeling of physiological control systems.

Aspects such as gender differences in blood pressure regulation, autonomic dysfunctions, orthostatic intolerance, microgravity, physical (exercise) training, high-g exposure and hemorrhagic shock are included. As LBNP duration and amount of LBNP applied lead to different responses across systems, there is a need to classify LBNP protocols based on the pattern of LBNP application (stepwise vs ramp), applied pressure and duration of application.

SPACE FLIGHTS ASSOCIATED CHANGES IN ASTRONAUTS PLASMA EEXOSOMES DERIVED RNA: BIOMARKER IDENTIFICATION

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During spaceflight, astronauts are exposed to stressors that have been linked to adverse effects on cardiovascular disease (CVD) associated morbidity and mortality. Circulating extracellular vesicles are selectively enriched in various RNA species that have great potential as predictive disease biomarkers. Our studies' main objective was to determine whether stress conditions in a space environment induce modifications in the exosomal miRNA contents, and these modifications can be used as preclinical prognostic biomarkers for health and disease.

To evaluate the potential impact of spaceflight environment on peripheral blood (PB) exosomes and their content, using small RNA sequencing, we systemically characterized circulating exosomal miRNA profiles from 5 astronauts PB plasma exosomes collected (STS-88 through STS-104) of 11–12-day space flight between 1998-2001) at two-time points – 10 days before the launch (L-10), and three days after landing (R3). Using state-of-the-art bioinformatics tools, we determine the predictive/prognostic biomarker value of space travel-associated modifications in exosomal contents of plasma samples.

Our experimental results suggest that low Earth orbit (LEO) space flights of 10-12 duration may induce a robust set of up or down-regulated miRNAs in the plasma exosomes derived from astronauts plasma. Further bioinformatics analyses identified that exosomal content in astronauts' blood could be used as a source of preclinical prognostic biomarkers. Specific genes that target up/down regulated small RNAs derived from astronauts PB exosomes, filtered by >2-fold change, false discovery rate adjusted P-value <0.05. The top ten differentially expressed miRNAs were associate with heart, kidney, and liver diseases. Cardiac diseases and functions represented more than 50 % of the mRNA targets regulated by up/down expressed miRNA (miR-10, miR-17, miR-23, miR-30, miR-181, miR-214, and MT-TY) derived from astronauts (PB) exosomes. The major heart disease and functions were represented by dilated cardiomyopathy, fibrosis of the heart, hypertrophy of the left ventricle, cardiac arrhythmia, cardiac arteriopathy, and myocardial infarction. In addition to the heart diseases, kidney and liver diseases

and functions were identified among the top 10 pathological effects by organ – kidney and liver diseases. Four select miRNAs (miR-10, miR-17, miR-23, and miR-30) are reported to affect all three organs, demonstrating widespread toxicity. Besides, miRNAs were associated with several biological function and pathway, i.e., angiogenesis and vasculogenesis (miR-10, miR-17, miR-23, miR-30, miR-154, miR-181, miR-214, miR328), the proliferation of vascular endothelial cell and migration/proliferation of tumors cells (miR-23, miR-134, miR-154, miR-181). qRT-PCR validation showed that most differentially expressed miRs are regulated in the same direction in individual astronauts. In particular, altered expression of miR-4485 may serve as a potential biomarker for the diagnosis of cardiac fibrosis and hypertrophy. We also validated the mRNA targets of identified miRs by transcriptional profiling of human cardiomyocytes and human microvascular endothelial cells treated with astronaut PB-exosomes.

This is the first of its kind small RNA-seq study, to date, for profiling astronaut's blood-derived exosomal RNA, suggesting that PB source for exosome isolation and identification of potentially predictive biomarkers for cardiovascular and other diseases.

DEVELOPMENT OF SOFTWARE FOR EVALUATION OF THE EFFECTIVENESS OF COUNTERMEASURES FOR NEGATIVE EFFECTS OF PROLONGED EXPOSURE TO WEIGHTLESSNESS

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Purpose. Comparing metabolic response while exercising in a microgravity environment and on earth and evaluating the impact of prolonged exposure to weightlessness on metabolism required development of software for analysis of the data collected during two sets of tests. Difference in energy expenditure, respiratory coefficient and anaerobic threshold were chosen as indicators of metabolic changes in question.

Methods. In the first set of tests, dynamics of oxygen consumption and carbon dioxide production were determined via metabolic measurement system 'Oxycon', as well as dynamics of heart rate, during the same training before and after the space mission. In the second set of tests, dynamics of heart rate during the treadmill interval training was recorded on earth and in weightlessness.

Results. Energy expenditure was calculated by both heart rate method and respiratory calorimetry for the first set of tests, and by heart rate method for the second set. The anaerobic threshold was calculated from the data collected during the tests conducted on earth, and was later used for evaluating the share of aerobic and anaerobic processes in energy expenditure.

Conclusion. The developed software enables calculating energy expenditure both from dynamics of heart rate and from dynamics of oxygen consumption and carbon dioxide production, as well as respiratory coefficient. It is planned to add other functions, such as more precise calculation of anaerobic threshold.

SEXUAL WELLBEING & SEXUAL SECURITY IN ISOLATION & CONFINEMENT ENVIRONMENTS

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As humanity treads further and further into increasingly extreme environments and for increasingly longer periods of time, questions concerning social, psychological, and physiological factors will become increasingly complex and pressing. Societal and political developments have seen women join astronaut corps and Antarctic teams since the 1960s. Since then, researchers have been keen to study gender-specific traits on both individual levels and in terms of group dynamics. Psychosocial research has taken a more prominent stance as scientists realize that these factors play a decisive role in mission success and safety.

Nevertheless, what is missing in this body of research is an examination of human sexuality in these kinds of extreme environments – a topic that has been avoided by many of the key organizations in the field despite sexuality being a driving component of the human condition and vital for the existence of humankind. There have been several incidences of sexual misconduct in extreme environments and in the age of #metoo, it is important that space agencies are armed with tools and knowledge to protect the sexual security and secure the sexual wellbeing of astronauts. We developed a preliminary research project focusing on sexual wellbeing and sexual security which now currently ongoing on the Antarctic station Concordia. The research is currently very exploratory and introductory in nature and aims to achieve an overview of the sexual issues that occupy humans isolated for 1-year missions on antarctic stations which serve as analogues for space habitats. By means of questionnaires, implicit association tests, and interviews, we hope to establish a foundation for further research into this neglected field of space psychology. With our presentation we aim to present our methodology, underline the importance of sexuality in behavioural space research, and discuss possible routes for future investigation.

We would like to thank the DLR for funding this experiment with the DLR grant 50WB1925 as well as ESA for providing us access to the crew at Concordia Antarctic Station.

NOVEL ANTIMICROBIAL FLEECE INHIBITS GROWTH OF HUMAN-DERIVED BIOFILM-FORMING STAPHYLOCOCCI DURING THE SIRIUS-19 ISOLATION

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Two novel antimicrobial surface coatings were tested for their lasting antibacterial effect under simulated space conditions during the SIRIUS-19 study. Because long-term space travel can affect the human immune system, astronauts are particularly susceptible to infectious disease. The space flight environment can alter the composition of microbial communities within the spacecraft and increase bacterial virulence and resistance to antibiotics. In addition to protecting the crew from infection by human pathogens, prevention and elimination of bacterial contamination is important to avoid corrosion and damage of the technical equipment. The antimicrobial coating AGXX® consists of micro-galvanic cells consisting of the noble metals silver and ruthenium which harm bacterial cells through the release of reactive oxygen species. Over the last years, several studies on the antimicrobial activity of AGXX® have demonstrated an effective inhibition of growth and even complete elimination of many pathogenic bacteria – including multi-resistant strains – as well as their biofilms. The second antimicrobial coating applied in the study, GOX, consists of chemically modified graphene oxide. Through a positive surface charge and its flexible scaffold, GOX can multivalently bind and immobilize bacteria via electrostatic interaction. In this study, the both coatings were applied to non-metallic carriers not tested before. AGXX® and GOX, as well as uncoated controls, were exposed in the SIRIUS habitat and analyzed at three different time points during the 4-months isolation study. Survival and growth of airborne heterotrophic, aerobic bacteria on the surfaces were assessed by culture-dependent methods, using growth conditions suitable for potential human pathogens. Human-associated Staphylococci (*S. hominis*, *S. haemolyticus*, *S. epidermidis*) strongly dominated at all time points. All isolates of biosafety level 2 formed biofilms and were resistant against at least one antibiotic. Most abundant were resistances against the antibiotics, erythromycin, kanamycin, and ampicillin. For most isolates, the respective resistance genes were assigned by PCR. Some of them were located on plasmids >20,000 bp thus likely facilitating their spread via horizontal gene transfer.

AGXX® coatings completely inhibited growth of these opportunistic pathogens on all tested surface materials, AGXX®-cellulose fleece showing the highest activity by a clear reduction in bacterial load able to recover post contact. GOX-cellulose fleece efficiently immobilized bacteria.

16S rRNA gene amplicon sequencing revealed that the isolated Staphylococci did not dominate the overall bacterial community, accounting for only 0.1–0.4 % of all sequences. Instead, molecular data revealed a higher diversity, with *Lactobacillus*, *Comamonas*, *Pseudomonas*, *Sporosarcina* and *Bacillus* as the dominant genera across all samples and time points.

THE E-NOSE BREATH GAS EXPERIMENT

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The E-Nose Breath Gas is a Russian-German experiment in the Russian segment of the International Space Station (ISS) to study changes in volatile organic compounds (VOCs) contained in the breath gas associated with oxidative stress. In preparation and during extravehicular activities (EVAs) cosmonauts aboard the ISS are exposed to excess oxygen (hyperoxia). Hyperoxia is assumed to increase oxidative stress and peroxidative damage to deoxyribonucleic acid, lipids and proteins on cellular level in the body. It was shown, that such oxidative processes are accompanied by the change of volatile organic compounds (VOCs) in the breath gas. Measuring the VOCs as biomarkers for oxidative stress may be a promising non-invasive diagnostic method to monitor the health status of cosmonauts affected by the adverse conditions in space. The experiment hardware is based on commercially available gas sensor products and comprises of a mask for breath gas sampling and a measuring device for sorbent tubes filled with the VOCs from the breath gas. The hardware is currently in the qualification for the usage on board the ISS. The experiment foresees to conduct measurements on 12 cosmonauts scheduled for EVA. Breath Gas measurements are conducted on ground before launch to and after return from ISS, periodically over the stay on ISS as well before and after an EVA. The E-Nose Breath Gas already demonstrated its performance, technology readiness and operability during a Biological Technological Test (BTT) conducted on 12 healthy volunteers by successfully detecting the oxidative stress in the exhaled breath as a reaction to breathing pure oxygen.

Breath profiling is a promising non-invasive method to observe biochemical processes in the body, particularly those related to diseases. Currently, an adapted E-Nose is used at the Medical Centre of the University of Munich/Germany to differentiate between bacterial and viral infections, thereby helping to reduce the overuse of antibiotics. With the rise of the COVID-19 pandemic in Europe early in 2020 the scope of the study was extended to apply the E-Nose in the detection of SARS Cov-2 infections.

The E-Nose is a compact, easy-to-use and sensitive device for non-invasive diagnostics or health monitoring using only a very low amount of consumables and without the need for a laboratory (like e.g. for blood samples or throat specimens). After a period of ~20 minutes the data is digitally available for further analysis. Future improvements should be oriented to further increase the sensitivity and/or reduce the sampling time (currently ~ 10 minutes). This would allow a near real-time monitoring of metabolic processes in the human body with shorter time scales like the effects of mental stress. Nowadays, mental stress is an important topic because continuous stress e.g. at work can cause mental illness and consequently a significant economic damage.

EEG COMPLEXITY FEATURES BASED MACHINE LEARNING DISCRIMINATES BETWEEN DIFFERENT MENTAL WORKLOAD STATES IN TERRESTRIAL AND LUNAR GRAVITY ANALOG

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As in this decade habitation of the moon will become feasible, assessment of the physiological adaptation to lunar gravity constitutes one major goal. Especially the functioning of the nervous system under such environmental challenge is of interest as it will crucially determine mission outcome. However, only limited information has been gathered on neuro-physiological functions in lunar gravity. In this study, we aimed to assess whether the complexity of the EEG was changed between different cognitive loading in a lunar gravity analog, and whether it was possible to differentiate between terrestrial and lunar gravity conditions.

Material and methods: The EEG of six right-handed young male volunteers were recorded while their head was either in the terrestrial (sitting upright) or in the lunar (9.5° head up tilt) gravity analog position. The participants stayed eyes-closed for 180-seconds, and performed then a 60-second "number subtraction" task. The EEG signals were epoched into 250, 500, 750, 1000, 1500, 2000, 3000 and 4000 ms time windows and the Approximate Entropy (AppEn) algorithm was applied to each window. Each windowed AppEn time series of the 16 EEG channels were used as input to machine learning and tested with 23 different classifier algorithms: Several variants of K-Nearest Neighborhood, Support Vector machines, Decision Trees, Quadratic and Linear Discriminant, Logistic Regression classifiers were implemented using 5-fold cross validation. Results: Both for the terrestrial and lunar gravity analog condition, the best classifier reached an accuracy rate over 90 % when discriminating the

eyes-closed state from the subtraction task. Post-hoc time-frequency analysis revealed beta-band enhancement in the left fronto-central area as a strong contrast when switching to the subtraction test. The discrimination of the terrestrial from the lunar gravity analog head position reached even classification scores over 95 % accuracy; this score was valid both for the eyes-closed and subtraction task. Classification accuracy was always higher for the longer time windowing. Calculation of sample and fuzzy entropy values yielded nearly identical times series as the ones for AppEn.

Conclusion. The classification of head positions and mental tasks with a high rates of accuracy values by machine learning algorithms using entropy metrices of EEG time series may provide an informative tool for assessment of cognitive functioning during lunar missions.

HABITATS IN EXTREME ENVIRONMENT AND HABITABILITY – A REVIEW

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The social, psychological and also spatial significance of living in an extraterrestrial environment place demands not only on the type of persons who would be 'best fit' to inhabit such environments but also on the living spaces that must be crafted to support human habitation in such environments. One of the critical characteristics for living and working in those environments – and thus mission success – is the dependency on the habitat, its technological capability as well as the capacity to counteract the stresses of a closed loop, extreme environment.

Historically, such habitats have lacked all but the merest attention to such details with a focus primarily on surviving rather than thriving. This is changing and the built environment is slowly becoming an important factor to ensure both physical and psychological wellbeing.

The authors have explored various concepts of the term *Habitability* for isolated, confined, extreme (ICE) environments from the perspectives of the inhabitants as well as the planners and social sciences. The authors span their research from early isolated and confined missions, to the first mockups and simulated habitats, through in-situ-environments and space habitats. They will provide an overview of the historic advancements of manned space craft, as well as highlighting various current and future concepts of 'habitability' and their translation into design.

THE PERCEPTION OF SELF-MOTION IN MICROGRAVITY

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Moving around in a zero-gravity environment is very different from moving on Earth. The vestibular system in 0g registers only the accelerations associated with movement and no longer has to distinguish them from the acceleration of gravity. How does this affect an astronaut's perception of space and movement? Here we explore how the perception of self-motion and distance changes during and following long-duration exposure to 0g. Our hypothesis was that absence of gravity cues should lead participants to rely more strongly on visual information in 0g compared to on Earth. We tested a cohort of ISS astronauts five times: before flight, twice during flight (within 6 days of arrival in space and after 3 months in 0g) and twice after flight (within 6 days of re-entry and 2 months after returning). Data collection is on-going, but we have currently tested 8 out of 10 participants. Using Virtual Reality, astronauts performed two tasks. Task 1, the perception of self-motion task, measures how much visual motion is required to create the sensation of moving through a particular distance. Astronauts viewed a target at one of several distances in front of them in a virtual corridor. The target then disappeared, and they experienced visually simulated self-motion along the corridor and pressed a button to indicate when they had reached the position of the remembered target. Task 2 was the perception of distance task. We presented a virtual cube in the same corridor and asked the astronauts to judge whether the cube's sides were longer or shorter than a reference length they held in their hands. We inferred the distance at which they perceived the target from the size that they chose to match the reference length. Preliminary analysis of the results with Linear Mixed-Effects Modelling suggests that participants did not experience any differences in perceived self-motion on first arriving in space ($p = 0.783$). After being in space for three months, however, they needed significantly more visual motion (7.5 %) to create the impression they had passed through the target distance ($p < 0.001$), indicating that visual motion (optic flow) elicited a weaker sense of self-motion than before adapting to the space environment. Astronauts also made size matches that were consistent with underestimating perceived distance in space (on arrival: 26.6 % closer, $p < 0.001$; after 3 months: 26.3 % closer, $p < 0.001$) compared to the pre-test on Earth. Our results indicate that prolonged exposure to 0g tends to decrease the effective use of visual information for the perception of travelled distance. This effect cannot be explained in terms of biased distance perception. Knowing that astronauts are likely to

misperceive their self-motion and the scale their environment is critical information for the design of safe operations in space and for readjustment to other gravity levels found on the Moon and Mars.

We acknowledge the generous support of the Canadian Space Agency (15ILSRA1-York).

NEW HUMAN NEURAL CELL MODELS OF LOW-DOSE SPACE-LIKE RADIATION EXPOSURE

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Statement of purpose. As space radiation biology progresses towards new countermeasures and improved risk quantification, we must have experimental models that bridge the gap between rodents and humans. This is critical for testing the mechanistic underpinnings of cellular and tissue responses such as those relevant to radiation-induced neural dysfunction. Past research has proven the value of developing human cell culture models for radiation research including cultures of hematopoietic stem/progenitor cells, vascular models, and neural/neuronal progenitor cells. Furthermore, *in vitro* models lend themselves to high throughput screening and are less expensive than are *in vivo* models. This work seeks to validate new experimental paradigms pairing three-dimensional neural culture with high energy and high precision particle accelerators.

Methods & models. The first of these combines the high physiological fidelity of mouse organotypic brain slice cultures (OBSCs) with the spatially precise radiation of Columbia University's Radiological Research Accelerator Facility (RARAF) particle microbeam to investigate the spatiotemporal response of microglia to focal radiation damage. This allows for the spatially resolved interrogation of the tissue relative to specific particle traversals, which sidesteps the common dose-rate problem of terrestrial models. The second combines a human neuron-astrocyte coculture model of Alzheimer's disease pathology [Kwak, S.S., Washicosky, K.J., Brand, E. et al. (2020) Nat Commun 11, 1377] with the high energy, mixed particle radiation of Brookhaven National Laboratory's NASA Space Radiation Laboratory (NSRL) to investigate the effect of radiation exposure on Alzheimer's pathology development. The third combines a human induced pluripotent stem cell (iPSC)-derived cell model with the NSRL particle accelerator to investigate how apolipoprotein E (APOE) allelic variants may alter radiation-induced neurodegenerative pathology. Thus far, we have interrogated model responses from 0.75 Gy to 2.0 Gy of gamma radiation and 0.5 Gy and 0.75 Gy of a 5-ion mixed particle radiation field at NSRL, which is termed the galactic cosmic ray simulation (GCRsim).

Results. Chronic effects of low-dose exposure can be small and difficult to detect. Indeed, we see no overt radiation-dependent changes in cell death or morphology. However, investigations with the human cell model of Alzheimer's disease pathology have yielded observations of radiation-induced alterations in the accumulation and processing of beta-amyloid (Aβ) protein. In a clear pattern observed across several experiments, the amount of insoluble Aβ increases with dose despite no increase in levels of its precursor protein. This suggests that the low-dose (0.5 Gy – 2 Gy; gamma and mixed particle) radiation response of these neural cultures impairs clearance of this protein. Furthermore, we are expanding this model to include the radiation response of microglia, which are sensitive to these low dose exposures. We have also achieved proof of concept testing with the OBSC and iPSC-derived models. These each present unique advantages that can be leveraged to further our understanding of the brain's response to space radiation.

NASA Human Research Program 80NSSC18K0810 (CAL); NASA Space Technology Mission Directorate 80NSSC17K0083 (RGH).

ORTHOSTATIC TACHYCARDIA AND FUNCTIONAL CARDIAC RESPONSE FOLLOWING STRICT HEAD-DOWN-TILT BEDREST

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Aims. Reduced physical activity increases the risk for heart failure, however, noninvasive methodologies detecting subclinical changes in myocardial function are not available. We hypothesized that myocardial strain measurements could capture subtle abnormalities in myocardial function secondary to physical inactivity.

Methods and results. In the AGBRESA study, which assessed artificial gravity through centrifugation as potential countermeasure for space travel, 24 healthy persons (8 women) were submitted to 60 days strict -6° head-down-tilt bedrest. Participants were assigned to 3 groups of 8 subjects: a control group, continuous artificial gravity training on a short-arm centrifuge (30 minutes/day) or intermittent centrifugation (6x5 min/day). We assessed cardiac morphology, function, strain, and hemodynamics by cardiac-MRI and echocardiography. We observed no differences between groups and, therefore, conducted a pooled analysis. Consistent with deconditioning, resting heart rate (Δ8.3 ± 6.3 bpm, $p < 0.0001$), orthostatic heart rate responses (Δ22.8 ± 19.7 bpm, $p<0.0001$), and diastolic blood-pressure (Δ8.8 ± 6.6 mmHg, $p < 0.0001$) increased, whereas cardiac-output (Δ-0.56 ± 0.94 l/min, $p=0.0096$) decreased during bedrest. Ejection fraction and left-ventricular mass-index did not change. Echocardiographic global longitudinal peak strain (Δ1.8 ± 1.83 %, $p < 0.0001$) decreased, whereas global MRI circumferential strain increased non significantly (Δ-0 .68 ± 1.85 %, $p = 0.0843$). MRI values rapidly returned to baseline during recovery.

Conclusion. Prolonged head-down-tilt bedrest provokes changes in cardiac function, particularly strain measurements, that appear functional rather than mediated through cardiac remodeling. Thus, strain measurements are of limited utility in assessing influences of physical deconditioning or exercise interventions on cardiac function.

PREDICTIONS OF HEART RATE AND OXYGEN UPTAKE DURING EXERCISE FOR ACTIVITIES IN SPACE

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Purpose. Heart rate (HR) and respiratory oxygen uptake (V'O2) kinetics can be determined by pseudo-random binary sequences (PRBS) work rate (WR) changes. This can be applied to plan countermeasures and physical activities in Space to optimize human and material resources. The aim of this study was to predict steady states and incremental WR responses by means of PRBS WR changes.

Methods. 13 subjects performed a complex exercise protocol which comprises a section with 5 min constant WR at 30 W and 80 W, 10 min PRBS WR changes between 30W and 80W and an incremental WR increase (INC, 25 W per min). From the PRBS part HR and V'O2 dynamic characteristics as impulse response, slope and offset were determined via time-series analysis. By mathematical convolution, a prediction for HR and V'O2 were calculated for the complete exercise protocol. The predictions for steady states at 30 W and 80 W and the individual correlations for the PRBS interval and the incremental part from 80 W to 175 W were calculated. Residuals between measured and predicted data were determined.

Results. The impulse responses confirm faster kinetics responses for HR than for V'O2 to WR changes. An average correlation coefficient between measurement and prediction was 0.64 ± 0.12 (HR) and 0.62 ± 0.09 (V'O2) for the PRBS and 0.91 ± 0.09 and 0.82 ± 0.07 for INC, respectively. Measured and predicted steady states for HR at 30 W (91 ± 11 bpm versus 95 ± 13 bpm; +4 % difference) and at 80 W (120 ± 16 bpm; 115 ± 15 bpm; -4 %) differed significantly. Similar but not significant differences were found for V'O2 (30 W: 0.71 ± 0.07 L min-1, 0.73 ± 0.07 L min-1; 4 % / 80 W: 1.18 ± 0.08 L min-1, 1.17 ± 0.09 L min-1; 1 %). Residuals showed relatively constant deviations for HR but increasing differences (= measured - prediction) with increasing V'O2.

Conclusion. It is possible to predict steady states from PRBS data within a range of ±4 %. The predictability for HR was better than for V'O2 which indicates deviations from WR-V'O2 dynamic linearity. Moreover, the resulting impulse responses imply deviations from simple first- or second order responses. This study showed that PRBS testing allows a characterization of HR and V'O2 kinetics and a limited prediction beyond the PRBS range. In the next step this idea should be tested in field situations to review the possibility to predict task performance and/or physiological load during physical activities in Space (e.g. extravehicular activities) as well as on moon or mars after long-term phases of microgravity.

PRBS KINETICS TEST AS TOOL TO DETERMINE EFFECTIVENESS OF PHYSICAL TRAINING

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Purpose. Kinetics of heart rate (HR) are an indicator for changes in physical performance. For reliable data, however, a testing close to typical activities after re-entering gravity is mandatory. Therefore, the application of a kinetics test protocol with pseudo randomized changes of moderate walking speeds on a treadmill in combination with incremental exercise is tested for feasibility on board the International Space Station (ISS) as well as pre- and post-mission is be investigated.

Methods. Five male cosmonauts (47 ± 3 yrs) were tested before and after the space mission on a treadmill, applying changes in speed in the form of pseudo random binary sequences (PRBS). 3 of these cosmonauts were also tested during space

flight. Oxygen uptake (only pre/post) as well as heart rate (HR) were measured, and time series analysis was used to obtain kinetics information. Higher maxima of the cross-correlation functions (CCF_{max}) between the applied velocity and the respective parameter indicate faster kinetics. The results were compared with training data of the cosmonauts during the mission.

Results. However, the initially slowed HR kinetics at the beginning of the mission slightly accelerate until the end of the mission. This designates the effectiveness of the applied exercise countermeasure towards the end of the mission. However, post-mission HR kinetics were slower compared with pre-mission data, indicating a loss in physical performance after the space mission.

Conclusion. The PRBS kinetics test on a treadmill was applicable to assess HR, a simple to acquire parameter during space missions. The exercise test of moderate intensity is feasible in the exercise test setting onboard the ISS. Moreover, this test can easily be integrated into training activities and the daily work schedule since it does not require maximal exercise intensities. In the future, the test should be used to predict exercise capacity after re-entry to gravity.

AEROSPACE SCIENCE POPULARIZATION EDUCATION

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Scientific popularization is one of the most important facilitating factors to realize the scientific and technological innovation. Aerospace science popularization education has been become an area of concern in space development nowadays, it stimulates the enthusiasm of human, especially the students, to learn aerospace knowledge. More and more different ages students begin to have great interests in aerospace, and there are many related organizations and schools starting this type of courses to teach the professional knowledge about aerospace, which meets the needs and enthusiasm of these students. However, the existing education problem about aerospace is that the educators only focus on showing the knowledge in the textbook, it may contribute to the result which is that students may get bored in the literal message, and they may lose the interest in aerospace. In addition, through the study of the textbook knowledge, they only memorize the basic meaning or theory without the authentic image about space in their brains. As a result, it is especially essential for the educator to think out a new way which is combine the knowledge with the practice to implement the aerospace science popularization education job.

This paper will introduce a new type of aerospace science popularization education, and give some examples to demonstrate its advantages. There are three methods to reach the new education goal.

The first one is to establish a complete curriculum system. Exactly, the detailed curriculum is the foundation of the science popularization process. Based on space knowledge, the course collects data and cases from the authentic space scenario, transforming it into a curriculum theme suitable for different ages, in the meanwhile, it also achieves the interdisciplinary practical course for students' quality building and interest expansion through inquiry. Besides the basic aerospace knowledge, the courses also contain some stories of the scholars in space area and aerospace heroes and heroines, such as the experience of Chinese scientist Tsien Hsue-shen, who had a great contribution to aerospace. These biography courses aim to carry forward and stimulate the spirit of spaceflight to the growing students. The second key point is organizing and carrying out some aerospace popular scientific activities. For example, through the several activities, the students of different ages could build up the rocket model through the team competition, and assembling the lunar rover is another handmade activity which the students can operate by themselves. The last one is to add an entirely new method of teaching, which is the virtual reality experience with aerospace content. Through the combination of space classroom learning and authentic space experience, students may step into space, revealing rockets, exploring the moon, traveling in space. This immersive experience process will bring a novel perspective through the learning. This teaching mode makes students who study the course not only learn professional aerospace knowledge, but also stimulate the self-operation fun of students.

At the end, this paper will analyze the disadvantages of this mode and explain the plans of the future development. As for the curriculum content, the teaching tools should be improved and the VR experience could be perfected in different attractive themes. In a word, the educators who are doing this job will put more effort into the aerospace scientific popularization, looking for an appropriate way to educate the children interesting in aerospace.

BIOMEDICAL RESEARCH IN ANTARCTICA AND HUMAN FLIGHTS INTO DEEP SPACE

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Space medicine from the first steps of its formation paid great attention to the conduct of terrestrial analog experiments to study the behavior and physiological state of the human body in conditions that simulate the effects on the body of separate

or cumulative factors of space flight and outer space. In 1966, the Institute of Biomedical Problems chose one of the analogue models the year's stay and the work of specialists of various profiles at the Vostok station located in Central Antarctica. The climatic parameters in the area of the station are close to cosmic. These are low temperatures (up to -89.2 °C), high UV radiation, lack of liquid water, high air ionization, reduced air content 02 in inhaled air, altered day-night cycle, absence of animal and plant life. The annual stay of people at this station takes place in isolation from the outside world, hypokinesia and hypobaric hypoxia. The crew of the station consists of 12–16 people. Our institute conducted biomedical research at Vostok Station during six Antarctic expeditions between 1966 and 1972. Then, after a hiatus, he resumed them in 2019. The purpose of these research is to study the patterns of human adaptation to long-term /up to a year/ stay in extreme conditions and to test the prophylactics means in relation to long-term of human orbital flights and flights to the Moon and Mars.

The results of psycho-physiological, physiological and biochemical studies revealed, as in space flights, the variability of changes in recorded parameters, which are not usually outside the normative values. Correlations of these changes with the climate seasons has not been established. Though the behavior and psycho-physiological parameters indicated the gradual development of asthenic syndrome in people. Experimentally established the effectiveness of taking anti-asthenic complex of pharmacological drugs and the feasibility of regular physical training in combination with hypoxia to maintain the overall functional state of the body in conditions of long-term isolation and hypokinesia.

Analysis of the results showed that the full adaptation of the physiological systems of the body to the conditions of a year's stay in the extreme conditions of wintering at the Vostok Station does not occur, although the state of the polar men by the end of one year wintering is assessed as quite satisfactory. Almost complete normalization of the studied biomedical parameters in the polar men of the Vostok station occurred two months after leaving the station and returning to the usual living conditions.

FEATURES OF DYNAMICS OF THE PROFESSIONAL OPERATORS AND VOLUNTEERS MICROFLORA IN ISOLATION EXPERIMENTS OF VARIOUS DURATION

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At present, it is more than obvious that various factors can affect the state of the microbiocenosis of a conditionally healthy person. The effect of extreme environmental factors on the human body is especially expressed during space missions. However, despite a fairly large number of works devoted to the study of the influence of space flight factors on human microbocenosis, the overwhelming majority of the studies were carried out before and after space expeditions. In this regard, ground-based models that simulate individual factors of a space flight play a key role in studying the influence of the factors.

One of the most promising models for simulating individual space flight conditions are isolation studies. In addition, of particular interest is the possibility of adaptation of crew members with different experience of participation in isolation experiments.

This study analyzes the data of microbiological studies of the microflora of professional operators and volunteers in isolation experiments of various duration, conducted at the Institute of Biomedical Problems, in order to assess the state of the microflora of the upper respiratory tract, intestines, and determine the most critical changes. In total, the data of 39 subjects, participated in 11 experiments were studied. When analyzing the results, the experience of participation of subjects in the experiments was taken into account. This made it possible to single out two groups: «professionals» (operators) and «beginners» (volunteers). In addition, for long-term experiments, the periods when visiting groups arrived at the «station» were taken into account.

The results were assessed in the form of an eubiotic index, which is the ratio of the number of positive changes in microflora to the number of negative ones, the total microbial count (TMC) and the proportion of some opportunistic microorganisms among all representatives of the microbiota of a particular biotope.

Data obtained on the microbiocenosis in operators and volunteers in isolation experiments of various duration, showed negative changes in the microflora of the upper respiratory tract and intestines. The eubiotic index decreased significantly during the period of acute adaptation in most experiments in both groups with a subsequent increase, but then underwent a decrease again, closer to the end of the experiment, which indicates that the microbial associations of the upper respiratory tract and intestines under conditions of an isolation experiment did not have proper stability. At the same time, operators negative changes were less critical than volunteers, which confirms assumption about the possibility of «addiction» to stress of volunteers who are not for the first time take part in isolation experiment.

TMC in visiting groups at the exit from the isolation chamber was lower than at the entering. Also, TMC-mouth, TMC-nose, S. aureus-nose in the visiting groups were significantly higher than those of the main crew, which indicates the active bacterial growth in these biotopes and an increased risk of developing dysbiotic states among members of the visiting groups upon arrival at the station.

The obtained data allow us to assert the need of correction of microflora using probiotic or autoprobiotic preparations from the first day of stay in the sealed compartment.

HUMAN PERIODONTAL TISSUES STATE DURING LONG-TERM ISOLATION IN CONFINED HABITAT

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The experiment was carried out as part of the international project SIRIUS.

The purpose of this work was to study tissues of human periodontium under conditions of 120-day isolation in confined object that simulates a short space flight.

A comprehensive study of periodontal tissues state included anaerobic component of the periodontal microbiota, immunological parameters in oral fluid and blood flow velocity in microvasculature (MVB) of the periodontium.

Samples were taken on the 14th and 1st days before isolation, during isolation 3 times every 30 days, after isolation 2 times (1st and 7th days) from 8 points using standard sterile swabs in 6 healthy subjects (3 women and 3 men) aged 29 to 45 years. All studies were performed on an empty stomach before teeth brushing. The qualitative composition of the main periodontal pathogenic species of microorganisms was determined by polymerase chain reaction method. Measurements of blood flow in the MVB of periodontal tissues were performed by ultrasonic Doppler fluometry (in the baseline, on days 1 and 7 after isolation). The dynamics of linear and volumetric indicators of blood flow velocities was assessed.

For statistical processing of research results, scientific-statistical package "Statistica v7.0" was used. After the end of isolation, there was an increase in linear indicators of blood flow velocity in the arteriolar ($p < 0.0007$), capillary ($p < 0.006$) and venular ($p < 0.004$) segments of the MCB of the periodontium relative to the background values. On the seventh day after isolation, there was a further improvement in the blood filling of the MCB capillary link in the periodontal tissues ($p < 0.00002$) relative to the background, ($p < 0.0002$) relative to the completion of isolation.

Presence of periodontal pathogenic microflora of the 1st order (Porphyromonas gingivalis) and 2nd order tissues (Prevotella intermedia). Was shown theis suggests etiological significance of these microorganisms to cause disease.

Analysis the oral fluid of immunoglobulins content, an increase reveals theis level on the 30th and 84th day of the experiment with a subsequent gradual decrease after experiment.

Thus, the revealed changes in local immunity and the presence of periodontal pathogenic microflora indicate a decrease in the protective mechanisms of the periodontal tissues. Along with this, a significant improvement in the indicators of blood flow velocity in the MCB of the periodontium was noted. Within the framework of the experiment, specialized toothpastes were used (two-component REMARSGEL complex), which could affect the improvement of the microecological balance of the microflora composition and the blood flow rate in the MCB of the periodontium. At the same time, the complex of factors associated with isolation, in turn, affects the development of negative changes in the periodontal tissues. Therefore, it remains possible to activate inflammatory processes directly in isolation.

SPACE RADIATION FACTOR DURING THE FLIGHT OF BIOLOGICAL SATELLITES

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A lot of space experiments with animals have been carried out before the first manned orbital flight. At present, space agencies of some countries carry out the projects aimed at launching crewed flights beyond the low Earth orbit: the flights to asteroids, circumlunar missions. Later on, the landing of the crew on the lunar surface is planned, followed by establishment of an astronaut-tended lunar base. One of the main precautions taken to ensure the safety of astronauts in interplanetary missions is biomedical radiation safety assurance under the exposure to the natural space ionizing radiation. Past and future space experiments on recoverable biological satellites can give necessary data for proper radiation risk estimations in the planned interplanetary missions.

The BION space program was started during USSR period. The purpose of the program was to carry our biological experiments in space flights. From 1973 to 1996 year 11 biological satellites were launched on low Earth orbits (apogee ~400 km, perigee ~200 km), rats and monkeys being main biological objects under study, the flight duration was from 5 to 22 days. In these flights, only integral absorbed doses were measured with thermoluminescent detectors. The typical dose rate was less than 0.3 mGy/day, that is lower than the dose rate in ISS compartments at the typical about 400 km near-circular ISS orbit.

Space biological experiments were continued in 2013-2014 years with BION-M1 and PHOTON-M4 recoverable satellite flights. The satellites were launched on April 19, 2013 and July 18, 2014, correspondingly at 64.9 degrees inclination orbits.

BION-M1 orbit was near circular at average altitude 575 km and flight duration was 30 days. PHOTON-M4 orbit was elliptical with 258 km perigee and 572 km apogee and the flight duration was 45 days. In these flights, not only integral dose but also the space radiation dose rate dynamics were measured by a special set of dosimetry instruments, the silicone detector included. Radiation quality factor and integral dose equivalent were measured by combining thermosluminescent and solid state nuclear track detector data. The measures integral dose in the biological satellites was as high as the typical ISS dose for a half a year flight.

Next flight of the biological satellite BION-M2 has been planned at higher circular orbit of 800 km altitude in September 2023. A new complex of modernized dosimetry instruments to be launched on BION-M2 will allow measuring not only integral doses and dose rate dynamics like on previous satellites but also linear energy transfer (LET) spectra from different space ionizing radiation sources at three different shielding depths. The space radiation dose in BION-M2 satellite for one month mission is expected to be as high as in the ISS typical orbit during 3 years.

The improved complex of the dosimetry instruments will make it possible to separate the received doses of space radiation by various components, such as electrons, protons, heavy charged particles and neutrons. Knowledge of the contribution from different components of space radiation facilitates correct modelling of the radiation effects on biological objects in ground experiments, making the model conditions as close as possible to the conditions of space flight.

No doubt, the radiobiological results that can be obtained on the biological satellites and in on-ground modelling experiments at particle accelerators are helpful for radiation safety issues of the future interplanetary missions.

HEAD DOWN BED REST EFFECTS THE PERCEPTION OF UPRIGHT: PERCEPTUAL SUPPORT FOR BED REST AS A MICROGRAVITY ANALOG

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Humans demonstrate many physiological changes in microgravity for which long-duration head down bed rest (HDBR) has proved a reliable analog. However, information on how HDBR affects sensory processing is lacking. We have previously shown (Harris et al., 2017) that microgravity alters the weighting applied to visual cues in determining the perceptual upright, an effect that lasts long after return. Here, we assessed whether long-duration HDBR has comparable effects. We assessed spatial orientation using the luminous line test (which yields the subjective visual vertical) and the oriented character recognition test (which yields the perceptual upright) before (once), during (three time) and after (twice) 21 days of 6° HDBR in 10 participants. By varying the orientation of the visual background and the relative position of their body and gravity (by having them lie on their backs and on their sides during bedrest as well as also being tested upright before and after HDBR) we were able to assess the relative weightings assigned to the contributions of the body, gravity and visual cues to upright. As with the effects of microgravity exposure, HDBR decreased the weighting of the visual cue relative to the body cue. The weightings returned to pre-bed-rest-levels by the second post-bed-rest-session. Before HDBR, vision had a measurably greater influence on the perceptual upright when supine compared to upright because a supine posture temporarily removes the effect of gravity from its normal effect along the long axis of the body. This increase gradually decreased during HDBR until no effect of posture could be seen immediately following HDBR. The subjective visual vertical, however, appeared unaffected by HDBR. This is one of the first demonstrations of a perceptual consequence of HDBR and further justifies its use as an analog for space. We conclude that bed rest can be a useful analog for the study of the perception of self-orientation during long-term exposure to microgravity.

Acknowledgements. Bed rest facilities were provided by the Institute for Aerospace Medicine at the German Aerospace Center (DLR) in Cologne-Porz, Germany. LRH and MJ were supported by Discovery Grants from the Natural Sciences and Engineering Research Council (NSERC) of Canada and funded by the Canadian Space Agency.

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SPACEFLIGHT-INDUCED MACRO- AND MICROSTRUCTURAL CHANGES IN THE BRAIN

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Introduction. Changes to the human brain as a result of spaceflight have only recently been uncovered in more detail. Most of these changes concern macroscopic changes in cerebrospinal fluid and cortical grey matter volume. We contributed to these emerging findings by performing the first prospective MRI study to investigate structural and functional brain changes after spaceflight, as well as the degree of reversal up to seven months after flight. Here, we report on both macro- and microstructural changes in cosmonaut brains after spaceflight using a state-of-the-art diffusion MRI (dMRI) analysis technique.

Methods. Thirteen male Russian Roscosmos cosmonauts (mean age (sd): 45 (4)) were enrolled in the study and were scanned 83 (32) days before launch and 9 (3) days after spaceflight lasting 171 (23) days. Nine cosmonauts received an additional scan at a follow-up time point 235 (60) days after return. dMRI data were acquired using an a priori defined sequence to perform the analysis of interest. DMRI data were corrected for several known artefacts using the standard MRtrix3 pipeline. Next, the apparent grey matter (GM), white matter (WM), and cerebrospinal fluid (CSF) volume fractions were estimated in each voxel of the brain, i.e. the resolution element of the MRI data, using multi- tissue spherical deconvolution. These tissue voxel fractions (VF) were also scaled by the local volume differences across scans, i.e. modulated voxel fractions (mVF). Changes in the VF metric reflects microstructural organisation within the voxel, while changes in mVF reflects net amount of tissue changes.

Statistical analyses were performed using nonparametric permutation tests with threshold-free cluster enhancement, comparing pre-flight, post-flight, and follow-up data through three paired tests. A threshold of $p < 0.05$, corrected for multiple comparisons using family-wise error (FWE) at the cluster-level, was applied.

Results. After spaceflight, we observe CSF VF and mVF decreases along the whole superior part of the brain and CSF VF and mVF increases along the inferior parts, as well as in the ventricles, as compared to preflight. These findings demonstrate a CSF redistribution around the brain, as well as ventricular dilation. GM VF, but not mVF changed in these same large-scale areas, but in the opposite directions, suggesting remodelling effects of the cerebral cortex due to the fluid redistribution, without a change in the amount of GM. Local increases in mVF of GM and WM were found in the basal ganglia primary motor cortex, and the cerebellum, indicating net tissue increases that are reflective of structural neuroplastic or adaptive changes in these three motor regions of the brain. Follow-up data reveals various degrees of return to pre-flight levels, with some inferior and ventricular regions showing persisting CSF increases in the longer term.

Conclusion. In conclusion, we find evidence for a CSF redistribution with concomitant GM remodelling changes, that are likely caused by the upward fluid shift and which corroborates with previous results. Furthermore, we find clear evidence of neuroplastic events taking place in three main motor regions of the brain, likely to subserve motor function adaptation.

SUSTAINABLE AND REVERSIBLE EFFECTS OF SPACEFLIGHT ON HUMAN BRAIN FUNCTION AND CONNECTIVITY

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Introduction. One pertinent question for human space travel is whether humans are able to adapt to the peculiar environment of outer space. Specifically, the brain harbours a tremendous capacity to adapt to altered bodily and environmental conditions, known as neuroplasticity. Therefore, we aimed to detect the occurrence of neuroplasticity though prospectively acquiring structural and functional data of the brain through whole-brain magnetic resonance imaging (MRI). Previous work has uncovered functional connectivity changes after spaceflight as revealed by a task-based functional MRI (fMRI) connectivity analysis. Here, we report on longitudinal resting-state fMRI connectivity changes observed in cosmonauts by scanning them before and after their mission to the ISS, with the additional inclusion of a long-term follow-up scan to assess the reversibility of these changes.

Methods. Fifteen male Russian Roscosmos cosmonauts (age mean (SD): 46 (5) years) were scanned 87 (32) days before launch, and 9 (3) days after Earth re-entry. Eleven cosmonauts received an additional follow-up scan 237 (52) days after re-entry. The average mission duration was 184 (49) days. 300 fMRI volumes were acquired (TE/TR=30/2000ms, 3mm isotropic voxel size, 42 slices) in eye-closed resting state. Standard preprocessing and denoising steps were performed to account for several known artefacts and sources of noise in the data. A hypothesis-free test by means of the intrinsic connectivity contrast (ICC; a metric reflecting the degree to which a voxel is functionally connected to all other voxels in the brain was used as an explorative global functional connectivity (FC) analysis. In each voxel of the brain, we investigated ICC changes after spaceflight compared to before that either sustain until the follow-up measurement seven months after the mission or return back to pre-flight levels. A whole-brain voxel-level threshold of $p < 0.005$ uncorrected was used, followed by a cluster-level threshold of $p < 0.05$ FWE-corrected.

Results. After spaceflight, sustained increases in global FC were found in the right angular gyrus (T=7.13, df=10, p(FWE)=0.042), while sustained decreases were identified in the posterior cingulate cortex (T=6.62, df=10, p(FWE)=0.016) and the thalamus (T=8.92, df=10, p(FWE)=0.021). The mid to anterior insular cortex in both hemispheres showed global FC decreases post-flight, which returned to pre-flight levels at follow-up (left insula: T=7.26, df=10, p(FWE)=0.003; right insula:, T=6.73, df=10, p(FWE)=0.011).

Discussion and conclusion. Resting-state functional MRI reveals FC changes after spaceflight, with some changes persisting for months after the space mission, while others return back to pre-flight levels. Changes were predominantly found in multimodal integration regions of the brain, pointing toward altered cerebral processing of bodily and environmental sensory signals. These observations could be explained by the altered sensory environment and related sensorimotor demands in weightlessness. On the other hand, previous findings from structural MRI showed signs of cortical remodelling and a CSF redistribution, which could be a potential factor inducing FC changes that needs to be further explored. Altogether, these findings provide, for the first time, evidence for brain functional connectivity changes to spaceflight and their effects up to seven months after return to Earth.

BIOFEEDBACK SYSTEM FOR ENHANCED MOTOR CONTROL UNDER MICROGRAVITY

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Introduction. Microgravity conditions are physiologically compromising and motor and fine-dexterity tasks involving the extremities including grasp and release are undermined, becoming delayed and placing greater force demands. Our group has recently developed an advanced model incorporating a sensorimotor platform that integrates sensing accelerometers. However, we described design specifications for 1-G conditions and these specifications must still be optimized for microgravity conditions. The mechanism of this model relies on the use of a tri-axial system, whereby sensors and controllers are utilized to detect and correct for key motor control elements consisting of 1) segment orientation, 2) motion compensation, and 3) inertial platform.

Methods. The novel accelerometer design utilizing our model was tested using MATLAB simulations and compared to existing gold standards for its sensitivity. Simulation modelling was based on crank-slider mechanism optimization, which uses predictive and output data to calculate position, crank velocity, and acceleration over time. We utilized available tracked prosthetic movement data with six DOFs and generated acceleration over time plots to compare the signal-to-noise ratio and drift between conventional accelerometers and our novel design. We additionally obtained dynamics data capturing translational movement along an X-axis, translation along a Y-axis, translation along a Z-axis, rotation around a roll axis, rotation around a pitch axis, and rotation around a yaw axis. This data included movement requiring segment orientation, motion compensation and an inertial platform.

Results. The results of the simulations for a calibrated conventional accelerometer model and our novel prototype design model demonstrated a significant difference in signal quality during segment orientation, motion compensation, and inertial platform. As a result, these algorithms can then used to generate command outputs in a prosthetic system. Of the two, our prototype was determined to reduce signal-noise effects observed in conventional accelerometers. Our modelling and prototype therefore demonstrates it is not only possible to mechanically dampen a system, but also that we can reduce noise and increase signal sensitivity by upgrading accelerometer design specifications.

Limitations and Future Avenues. While promising, this model has certain limitations: (i) it is a proof-of-concept and only been tested via simulation and must be further evaluated in varying microgravity conditions, (ii) our simulation focuses on two main accelerometer subtypes in modelling signal, (iii) considerations must still be made for mass and design of an incorporated and functional spacesuit system, and (iv) model needs to be enhanced for six or more degrees of freedom for maximal motor control.

MENTAL HEALTH IN PROLONGED SPACE TRAVEL

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Current research has identified areas of improvement for human emotional well-being on space missions, determining that: (i) current mental health training achieved from recording orbital spaceflight and simple conditions are not adequate to survey mental health into space and (ii) such stressful and prolonged missions must consider an individual's adjustment and execution, team communications, and ideas and strategies for mental countermeasures. In the Mars-500 venture, six crewmembers were set in an ecological environment that simulates the capacity of long space transport. During the mission, psychological, behavioral and other stresses among all members were recorded demonstrating increased manifestations of sorrow, altered rest wake cycles, sleeping disorders and physical weariness. Moreover, concerns such as long periods of separation from support networks, increased periods of stasis, prolonged habitation in a flight environment, reliance on robotics and technology, levels of seclusion, feelings of imprisonment, and social isolation were reported by crewmembers. These findings have been supported by a number of studies. NASA, and other national and international space organizations have focused on exhaustive physical and mental assessment procedures to screen individuals prior to missions for their vulnerability to these stresses. However, we suggest that there is a need for a shift in focus to ensuring enhanced mental health training, simulation, and supports for flight missions.

PRESSURE COMPRESSION BANDAGES FOR THE TREATMENT OF POSTURAL HYPOTENSION FOLLOWING RE-ENTRY

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Nearly all astronauts experience postural or orthostatic intolerance after space flights with approximately twenty percent experiencing syncope or presyncope after re-entry and landing. Syncope is characterized by a loss in consciousness resulting from an inadequate supply of blood to the brain whereas presyncope does not result in a loss of consciousness but still involves symptoms such as dizziness, vertigo, blurred or tunnel vision, nausea, headache, or sweating. The underlying cause of these conditions is the sudden shift from microgravity conditions to gravity on a celestial body – a common phenomenon in several space flights. Microgravity can induce hypovolemia, a condition where astronauts lose a great deal of their blood volume and thereby influence orthostatic tolerance.

There have been several proposed physiological mechanisms for this body fluid volume loss in microgravity conditions. One widely accepted theory suggests the reduction of a relatively unidirectional gravitational pull enables an increased fluid filtration in the upper body interstitial spaces. Another theory puts forward the peripheral vascular resistance becomes ineffective in microgravity such that there is an imbalance in perfusion leading to a lower preload to the heart. Both space flight and ground-based experiments have demonstrated the inability to provide proper peripheral vasoconstriction may be associated with reduced sympathetic nerve activity, arterial smooth muscle atrophy, arterial smooth muscle hyporeactivity, or hypersensitivity of beta-adrenergic receptors among others. Disregarding this mechanism however, hypovolemia will result in cardiac atrophy which weakens the heart and ultimately results in lower blood pressures affecting the orthostatic balance. Here, we propose compression bandages for the management of postural hypotension during re-entry.

The application of pressure compression bandages in the management of orthostatic intolerance is not a novelty. In fact, its use is mundane in the elderly to prevent progressive orthostatic hypotension, which is an increasingly common occurrence in the geriatric population during standing. Lower limb compression bandages, in particular, have been demonstrated to be effective in avoiding orthostatic blood pressure reductions.

We propose the use of pressure compression bandages would reduce microgravity-associated hypovolemia and increased blood loss in the upper body. There may also be a hidden utility for abdominal or upper extremity compression bandages in spaceflight. A clear advantage of compression bandages over pharmacological management is its focus on prevention. Moreover, compression bandages are both resource-efficient and low-cost. While promising however, relies extensively on several underlying assumptions and must account for several conditions for its feasibility.

THE EFFECT OF ELECTRICAL STIMULATION OF RAT HINDLIMB DURING 1-DAY MECHANICAL UNLOADING ON KCC2 PHOSPHORYLATION IN MOTONEURONS AND ANABOLIC AND CATABOLIC MARKERS IN SOLEUS MUSCLE

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It is known, that rat hindlimb suspension immediately leads to the elimination of electrical activity in rat soleus muscle. However, it was shown that starting from the third day of hindlimb suspension, soleus muscle electromyographic activity slowly increases, reaching the control level by the 14th day of exposure (Alford et al, 1987; De-Doncker et al., 2005).

In the current work, we hypothesized that an increase in the electromyographic activity in rat postural muscle during mechanical unloading could be associated with downregulation of potassium chloride co-transporter (KCC2) in motoneurons. Using electrical stimulation of rat soleus muscle during early unloading, we aimed to assess the activity of KCC2 in motoneurons as well as to estimate the state of the key anabolic and catabolic intracellular markers in soleus muscle.

Wistar rats were divided into three groups: 1) vivarium control (C); 2) 1-day hindlimb suspension (HS); 3) 1-day HS + constant low-intensity electrical stimulation of soleus muscle (20 Hz, 2 times for 4 hours) (HS+S). Mechanical unloading for 24 hours alone and electrical stimulation during unloading did not affect the cross-sectional area and the composition of muscle fibers. Electrical stimulation of the rat hindlimb did not affect the increase in the expression of E3 ubiquitin ligases MuRF-1 and Atrogin-1 caused by 1-day unloading, but significantly reduced ubiquitin mRNA expression. A decrease in the expression of ribosome biogenesis markers due to 1-day HS was not prevented by 8-hour electrical stimulation. Electrical stimulation during HS did not affect changes in signaling molecules involved in the regulation of translation initiation, as well as protein synthesis. Electrical stimulation during 1 day HS led to a significant increase in KCC2 phosphorylation (Ser 940) in motoneurons in the lumbar spinal cord.

Based on this data, it can be concluded that low-intensity electrical stimulation during 1 day mechanical unloading induced KCC2 activation in motoneurons and, accordingly, could contribute to the suppression of unloading-induced spontaneous tonic activity. In addition, the application of low-intensity electrical stimulation partially prevented unloading-induced upregulated expression of ubiquitin.

This work was supported by the RFBR grant No. 20 34 70022.

ENHANCING SYNAPTIC PLASTICITY IN VITRO USING NOVEL KETAMINE DERIVATIVES

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Decrease in cognitive performance is a frequently observed phenomenon in astronauts participating in long-term space missions. With the aim to pave the way for safe human space exploration, the development of pharmacological interventions to prevent or even reverse the decline in cognitive function is becoming more and more pervasive. We propose that novel pro-neuroplastic compounds developed by us and our partners can enhance synaptic plasticity and might thus be used as a countermeasure against potential neurodegenerative events during spaceflight.

Impaired synaptic plasticity constitutes a hallmark of cognitive performance loss. Ketamine, a drug applied for analgesia in emergency medicine and in treatment-resistant depression, and some of its metabolites rapidly induce synaptic plasticity. However, ketamine cannot be reasonably applied as a neuroprotective agent given its side-effect profile. With the aim to dissociate pro-neuroplastic actions from NMDA receptor-mediated psychotropic side effects we studied novel ketamine derivatives in vitro. We applied ketamine and different ketamine derivatives at various concentrations and incubation durations to primary hippocampal neurons cultivated until maturity of synaptic development. VAMP-2 immunostaining served as a measure for pre-synaptic density. For treatment with several candidates, e.g. compound HW-273, pre-synapse number was enhanced in a concentration-dependent manner. Furthermore, enhanced intensity measures of post-synapse immunostaining for GluA2 (AMPA subunit) in compound-treated cells indicated elevated AMPA receptor activation at low doses (0.5-1 μM), whereas for ketamine a higher dose was required for comparable effects. In addition, treatment with high compound concentrations showed no obvious cytotoxic effects, opposite to treatment with ketamine.

We conclude that novel ketamine derivatives potently augment neuronal plasticity in a concentration-dependent fashion which is independent from NMDA receptor engagement. In future studies we want to investigate whether these effects also apply to neuronal cells which are exposed to different gravity loadings.

Our study paves the way for the development of new neuroprotective therapies with less unwanted side-effects, which could benefit space travelers as well as individuals on Earth.

PSYCHOLOGICAL AND INTERPERSONAL ISSUES IN SPACE: ON-ORBIT, MARS, AND BEYOND

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Psychological and interpersonal research studies conducted on the Mir and International Space Stations and during Mars-relevant space simulation activities on Earth, such as the Mars-500 project, have examined a number of behavioral stressors that can affect crewmembers working in space. These include: isolation and confinement, danger, workload demands, personality conflicts, leadership roles, time effects, crew heterogeneity, national and organizational culture, and the crew-ground relationship. These stressors can affect crewmember well-being, crew cohesion, and communication with the ground, and they can lead to psychiatric problems and asthenization. Positive influences also affect crewmembers in space, such as the salutogenic impact of Earth observation and the Overview Effect. Countermeasures involving selection, training, and support from the ground have assisted crewmembers during on-orbit and lunar space operations, and these missions largely have accomplished their goals.

A Mars expedition will introduce new psychological and interpersonal stressors related to the extreme distance and duration of the mission. Crews will be more autonomous and dependent on local resources, communication delays will cause asynchronous interactions with mission control and family members on Earth, and the disappearing Earth phenomenon may produce a profound sense of isolation and impede the visualization of our home planet as a source of support. Mission control will have to adjust to changing work realities. The long duration and media attention related to the first Mars expedition will create challenges for crewmembers reintegrating with family and friends after returning to Earth. New countermeasures will need to be developed to deal with these stressors, such as efficient methods to improve asynchronous communication with home, periodic "bull sessions" to deal with crew tensions, and virtual reality or access to a telescope to view the Earth.

Looking further into the future, interplanetary missions beyond Mars and interstellar missions to exoplanets raise issues related to the need for speedier propulsion systems, suspended animation, and multigenerational star ships. The impact of the Earth-out-of-view phenomenon; commerce related to tourism, mining, and other space operations; and the permanent colonization of distant moons and planets, which are the stuff of science fiction, will become science fact in the post-Mars era.

In this presentation, Professor Kanas will discuss these issues and review some of the psychological and interpersonal research findings that have accrued from studies of on-orbit missions. Based on these findings, he will propose countermeasures for a Mars expedition and extrapolate our empirically-based knowledge to future manned space missions to the outer solar system and beyond.

THE EFFECT OF PHYSICAL ACTIVITY ON BLOOD PLASMA PROTEOME IN 21 DAY HEAD-DOWN BED REST

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Head-down bed rest (HDBR) is a ground-based experiment that is widely used to model the microgravity effects of spaceflight. Under these conditions, interdependent reactions from various body systems occur. The analysis of the potential effectiveness of exercise countermeasures under bed rest conditions is also useful in the studies of aging and post-traumatic injuries. A blood test using a panoramic proteomic method will help to identify the effects of HDBR in a comprehensive manner, without reference to any one organ or tissue. All tissues are washed with blood, so any physiological changes are reflected in changes in the proteomic composition of the blood. Thus, the aim of the study was to compare proteomic data on the effects of HDBR with or without countermeasures on the human body.

Eight healthy men (20–45 years old) participated in the experiment with head-down bed rest for 21 days with an angle of inclination of the longitudinal axis of the body relative to the horizontal position of 6°. HDBR was organized by the Institute of Space Medicine and Physiology (MEDES-IMPS) in Toulouse, France. Samples were collected one day before and on the 21st day of HDBR. All the volunteers participated in the control session of HDBR without countermeasures, and in the session with resistance vibration exercises comprising of squats, single leg heel and bilateral heel raises (RVE). Between sessions, the break was 4 months. Blood plasma was analyzed using liquid chromatography – mass spectrometry method based on a nano-HPLC Dionex Ultimate3000 system and a MaXis 4G.

Using MaxQuant and Perseus programs, 239 proteins were quantified in blood plasma samples. It was found that physical activity during HDBR modifies the plasma proteome, as compared with HDBR as such. So, in RVE samples the total number of significantly changing proteins decreased, which indicated the clinical effectiveness of this complex of preventive measures. The significantly different proteins of two groups of samples (HDBR and HDBR+RVE), were involved in such processes like regulation of proteolysis, fibrinolysis, platelet degranulation, complement activation, inflammatory response. The difference between processes of two sessions of HDBR was the appearance of such processes like regulation of glucose metabolic process, negative regulation of hydrolase activity, blood vessel endothelial cell migration, and disappearance of processes of regulation of blood vessel diameter and angiogenesis in HDBR+RVE.

In general, a similar, although less pronounced, response of the physiological systems of the body to the effects of HDBR was observed, despite the use of preventive measures. The main difference was a predominant effect on the processes of regulation of carbohydrate metabolism in the group with the use of preventive measures in the form of physical activity.

The work was carried out within the framework of the basic theme of the Russian Academy of Sciences 65.3.

MANIFESTATION OF HEMORRHAGIC SYNDROME AFTER HEAD-UP TILT TESTS IN 21-DAY DRY IMMERSION IN THE FORM OF PLASMA PROTEOME MODIFICATION

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The effect of the rapid redistribution of blood during head-up tilt tests in 21-day «dry» immersion suddenly became relevant in connection with the occurrence of mild hemorrhagic syndrome in the study participants. It became necessary to analyze the processes of occurrence of hemorrhagic syndrome as orthostatic and congestive purpura. The aim of this work was to study the features of the proteomic response of the human body to the rapid redistribution of blood during head-up tilt tests during 21-day immersion, which led to stagnant and orthostatic purpura.

Ten healthy men (23–34 years old) participated in the experiment with dry immersion for 21 days. The experiment was organized by the State Scientific Center of the Russian Federation - IBMP RAS. According to the program of the experiment, on the 7th, 9th, 14th and 19th days of immersion exposure, passive head-up tilt tests were carried out. Venous blood samples were collected 7 days before the experiment and on the 21st day of immersion. Blood plasma was analyzed in triplicate using liquid chromatography – mass spectrometry method based on a nano-HPLC Dionex Ultimate3000 system and a MaXis 4G. For bioinformatic analysis, the software packages Perseus and ANDsystem were used.

All subjects, starting from the 9th day of the study, after the head-up tilt test, had petechiae, pitting edema and swelling on the dorsum of the feet, ankles, and the lower third of the shins. Such symptoms indicate a combination of signs of venous insufficiency and diffuse dilatation of microvessels. Analysis of the blood proteome indicates a significant change in a number of proteins as a result of exposure to a complex of immersion factors. Using the ANDsystem program, a group of 6 proteins directly associated with vascular damage was determined. The main processes associated with orthostatic vascular purpura in "dry" immersion are the activation of fibrinolysis, platelet aggregation and response to vascular injury. One of significant processes was the process of regeneration, which could occur in case of damage to blood vessels as a result of the action of a complex of factors of «dry» immersion. Thus, at the molecular level, signs of damage to the microvasculature under the influence of simulated weightlessness with tilt tests were revealed. These findings are confirmed at the tissue level.

The obtained data are of scientific and practical interest in the direction of stratification of the risk of secondary hemosiderosis and evaluation of new treatment methods aimed at reducing reperfusion damage to soft tissues and parenchymal organs.

The work was carried out within the framework of the basic theme of the Russian Academy of Sciences 65.3.

MODELING OF EEG SIGNALS VIA PARTIAL DIRECTED COHERENCE AND DEEP LEARNING FOR THE IDENTIFICATION OF SUITABLE ARTIFICIAL GRAVITY LEVELS IN A SHORT ARM HUMAN CENTRIFUGE AS PART OF REHABILITATION OF PATIENTS WITH NEUROLOGICAL DISORDERS

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Exercise is an important aspect of the continuum of rehabilitation for individuals with neurological disorders. Exploitation of technological advances may function as an asset during this process. The Short Arm Human Centrifuge (SAHC), which is a well-established technology in aeronautics research field, is embedded in rehabilitation studies. Personalized approaches could have a positive impact and should be taken under consideration. Our objective is to identify the most efficient SAHC level per patient. We employed electroencephalographic (EEG) data recording during lying and standing posture as well as tasks of different artificial gravity levels on the SAHC. The data acquired from a healthy control group make up a total of 517 standing and 528 lying eeg segments, 16s duration each. Our analysis involved cortical functional connectivity estimation within various electroencephalographic rhythms (alpha, beta, delta, theta and gamma) through Multivariate Autoregressive Modeling (MVAR) and Partial Directed Coherence (PDC). Features obtained by analyzing lying and standing tasks were used as multidimensional images to train a binary classifier based on 2D Convolutional Neural Networks (2D-CNNs). The cross-validation accuracy of the proposed method is 88.23 ± 2.44 % which indicates the capability of providing adequate discrimination between lying and standing tasks. Hence, we propose that our methodology could be used to correlate brain activity during tasks of different artificial gravity levels on SAHC with that of lying or standing posture.

ISS – THE PREDICTION PLATFORM FOR EXPLORATION MISSIONS EVA PERFORMANCE

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Introduction. Prolonged zero-gravity exposure causes changes in the state of functions of gravity-dependent systems, which leads to a decrease in human performance after space mission completion. Changes in the central and peripheral parts of the neuromuscular system and the system of vegetative support for human muscle activity can lead to difficulties in cosmonauts' movement in a spacesuit on a planet surface immediately after landing. In this regard, it is important to compare emerging hypogravitational disturbances during a long space flight with the performance of typical extravehicular activities (EVA).

Purpose. To develop a set of techniques for detecting hypogravitational disorders associated with cosmonauts' performance of professionally-oriented test tasks before, during and after ISS missions, to predict the ability to perform model tasks critical for exploration missions success.

Methods. A general scheme of conducting a complex experiment is being developed. Cosmonauts' professional task performance before and after ISS expeditions will be correlated with the level of cosmonauts' physical performance before, during and after a long space mission to the ISS. The model research complex «Pilot-T» was considered as a prototype of the testing method of typical activities. Methods of expert assessment of space suit movement performance are being developed to correlate the assessment indicators with the parameters of body response to physical activity and treadmill walking locomotion pattern.

Results. Preliminary results of pilot experiments are presented. All models are being worked out with the participation of cosmonauts before, during and after the completion of the flight to the ISS lasting from six months to one year. The importance of taking into account the countermeasures system to the negative effects of spaceflight when predicting the success of EVA on the planet is shown. Among the priority areas of research, it is considered to set field experiments on Earth using several modeling complexes: stands for gravitational unloading of cosmonauts in spacesuits for spacewalking; stands for manned spacecraft rendezvous and docking; centrifuges with operating models of landing modules; computer stands with virtual models of EVA transport systems.

Discussion. The successful performance of exploration tasks will be partly determined by the influence of long-term spaceflight factors on a human and the prevention methods of the adverse effects of these factors. Complex studies using models of crew activity in conditions that reflect planning specifics of the activities sequences and their procedural features as accurately as possible are now a key element of developing technologies for the exploration of the Moon and Mars

Conclusion. The results of the pilot experiments revealed the importance of maintaining the mobility of a cosmonaut on the surface immediately after landing. The use of EVA transport systems can become a reserving factor in cases of emergencies during cosmonaut movement in a spacesuit. The prediction of the success of spaceflight missions is proposed to be based on the results of typical activities testing, the quality of which depends on the functional state of gravity-dependent physiological systems before, during, and after the flight.

KEY PREDICTORS TO SUCCESSFULLY COPE WITH THE YUKON ARCTIC ULTRA: THE LONGEST AND THE COLDEST ULTRAMARATHON

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Background. In recent years ultramarathons, i.e. distances longer than 42.195 km, gained rising interest among ultra-endurance athletes. Key predictors of a successful ultramarathon finish are still unknown. Neuropeptide Y (NPY), leptin, and adiponectin are known to be involved in resilience reactions and energy homeostasis and might influence a runner's success. Purpose of the present study was to explore the association between them and stress-related conditions.

Methods: The study involved 31 participants and seven control (19 men, 17 women, mean age 38.64 ± 9.12 years) during the Yukon Arctic Ultra (690 km course, temperatures between + 10.6°C and – 47°C). Data were collected at baseline (Pre), after 277 km (D1), 383 km (D2), and post-race (Post, 690 km). Standardised questionnaires were used to assess ratings of perceived exertion (RPE), total quality of recovery (TQR), and profile of mood states (POMS). Further parameters examined included blood levels of NPY, leptin, adiponectin, cortisol, sleep duration, and skin temperature (Geneactive and Senswear), and antioxidants level (Biozoom).

Results. Data of finisher (FIN, n = 10), non-finisher (NON, n = 19), and control (CON, n = 7) were compared. At Pre, leptin levels in NON (mean: 7.5 ± 9.39 ng/ml) and CON (mean: 9.04 ± 5.33 g/ml) were higher compared to FIN (mean: 5.23 ± 4.23 ng/ml). During the race, the leptin level varied in FIN, NON and CON significantly (D2: p = 0.045, Post: p = 0.028). In comparison between before and after the race, the leptin level in FIN decreased by 65.01 %. By contrast, the leptin level in CON increased by 29.87 %. Leptin significantly and positively correlated with RPE (0.78***), confusion (0.81***), fatigue (0.54*), and negatively correlated with TQR (- 0.91***). In FIN, NPY was higher (mean: 8.63 ± 5.43 µg/ml) compared to NON (mean: 7.57 ± 5.75 µg/ml). NPY increased during the first part of the race (Pre to D1) in FIN by 65.12 % (mean: 14.25 ± 8.64 µg/ml)

and in NON by 75.96 % (mean: 13.32 ± 6.63 μg/ml). The influence of NPY on mood states varied throughout the race and the group. Higher levels of NPY decreased the level of anxiety and depressive mood significantly. At D2 in all groups, the level of NPY correlated positively with the level of antioxidants (pre-sleep: 0.84***, post-sleep: 0.93***). By the end of the race and at Post, NPY positively correlated with adiponectin and leptin, indicating an interplay between them. There was a significant difference in sleep ratio between the FIN (mean: 40.60 ± 16.26) and NON (mean: 13.23 ± 10.33, p = 0.035). The FIN (mean: 19.72 ± 7.79) mean skin temperature was significantly higher than of NON (FIN mean: NON mean: 16.82 ± 9.78***).

Conclusion. Successful ultra-runners seem to have a fundamental prerequisite and the right composition of key factors improving resilience and perseverance. This might be due to the release of the right mix of neuropeptides and hormones based on genetic talent or due to a particular way of exercising.

INFLUENCE OF A FEMALE GENDER ON THE EFFICIENCY OF WORK IN A CREW OF MANNED SPACECRAFT

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Prospects for the development and exploration of space are relevant at any time.

One of the goals in the development of the space industry is the relocation of people from our planet.

Many prominent scientific thinkers, including the physicist Stephen Hawking, have argued that colonizing other worlds will be critical to the survival of humans and other species on Earth.

On the eve of the anniversary of Yuri Gagarin's flight, Roscosmos announced plans for the exploration of the Galaxy. Among the ambitious goals are flights to the Moon by 2030, building a base, and mining. The moon is the most natural and accessible site for extraterrestrial colonization.

Women play an important role in space exploration.

Interest in the peculiarities of the behavior of the female body in space arose at the very beginning of the space era – with the flight of Valentina Tereshkova. The experience of accomplished space missions of crews from different countries with the participation of women demonstrates the absence of serious psychological problems and disagreements during flights. Research shows that there are no fundamental differences between men and women.

Scientists are increasingly saying that in space flight in unfavorable conditions for long-term living in a pressurized facility, it is preferable to work with crews mixed in gender. According to the analysis of communication of the crew of a mixed gender composition in the SIRIUS-19 experiment, the manifestations of the phenomenon of «detachment» in the communication of the subjects with the control center, revealed in the Mars-500 project, were confirmed: a decrease in the volume of communication, a decrease in statements about needs and problems. Revealed significant differences in communication styles. A subgroup of women more often than a subgroup of men informed the Earth about problems, made requests, and communicated more emotionally. In the subgroup of women, more emotions of joy and sadness were observed. The subgroup of men was more likely to report anger that coincided with discussion of problems. Such manifested traits of a woman emphasize her need as a member of the crew.

The most beneficial from the point of view of a healthy working atmosphere, communication interaction and work efficiency are such teams in which women are present. The exact ratio (equally with men, 20 % to 80 % according to the Pareo principle or others) has not been unequivocally determined, but observations show that in a team mixed by gender, men and women show better self-organization, discipline, responsibility, and ability to work. In flights remote from the Earth, where the crew will work autonomously, relying only on themselves, the need for safe, comfortable and high-quality crew work increases.

By their very nature, women are characterized by enthusiasm, politeness, in reactions to stress – caring and mutual support, which is probably caused by an increased level of the hormone oxytocin, which is responsible for affection and trust in other people. In men, the level of the hormone adrenaline is increased, which is responsible for the speed of reaction in stress. A man is by nature dynamic, straightforward, a woman is characterized by such qualities as tolerance, gentleness, caution, flexibility in thinking, attentiveness, sensitivity – which balances the manifestations of men. Feminine nature is maternal, aimed at creation, bringing into harmony, smoothing out conflicts. In addition, the different types of thinking in a heterosexual carriage allow you to apply different approaches to solving issues and make a high-quality sample of them.

A man and a woman in the same carriage are specialists who are united by a single mission and perform common tasks, complement each other, together representing the strength that should be used in the effective achievement of common goals.

GAGARIN'S HERITAGE IN MUSEUM COLLECTIONS OF RUSSIA

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The topic of space exploration and the history of space achievements, the formation of the cosmonauts' personalities is presented in various sections in most of the local historical and scientific museums of the country. According to the public organization «Association of Cosmonautics Museums», more than 100 museums of Russia directly relate themselves to the space profile, that is, they are the keepers of the collections that reveal the history of space exploration.

One of the most important date for the Cosmonautics is a day when Yuri Gagarin became the first to take this step to the stars. April 12, 2021 will mark the 60th anniversary of the day when the human dream of flying into the universe was realized. The Russian museums with space expositions have paid great attention to this event over the past 60 years. The main purpose is to show the flight of Y. A. Gagarin as the greatest event and the greatest scientific and technical achievement in the history of mankind, which rises above time, leaves a deepest mark in the minds of contemporaries and influences the mindset of future generations, inspiring them to serve the highest ideals.

The Museum of Cosmonautics (Moscow), being one of the largest space museums in Russia, has prepared a unique exhibition project «The First One» for this event. For the first time, one exhibition will show authentic artifacts related to the life of Yuri Gagarin, the preparation and implementation of the world's first space flight. Along with the items from the collections of the museums and leading rocket and space enterprises, the rarities provided by the family of Yuri Gagarin will be displayed as exhibits. Among the 110 original exhibits are the lander of the first spacecraft «Vostok-1», the spacesuit «SK-1», a graduation work (a cast-iron grating cast by a student of the Saratov Industrial Technical School together with Yuri Gagarin), a student desk and awards, documents, letters, and personal belongings of the First Cosmonaut. In this composition, the specified memorial exhibition will be shown for the first time in Russia.

The unique exhibition begins with two artefacts dating from 1934. This is the book «The rocket flight into the stratosphere» - the only lifetime edition published under the name of the author S.P. Korolev. Another document is the «Birth Certificate», which states that on March 9, 1934, a son, Yuri, was born in the family of Anna Timofeevna and Alexey Ivanovich Gagarin. Korolev and Gagarin met in 1960. Fate gave them 6 years to go through life side by side. On April 15, 1961 the First Cosmonaut came to the Chief Designer, to the secret Special Design Bureau «OKB-1» with gratitude to the creators of the first space vehicle for its reliability, which did not fail. This event concludes the exhibition «The First One».

The museum artifacts of the Gagarin's heritage are stored and displayed in different places: in museums of the towns where Gagarin's formation as a person took place, where he was born, studied and served in the military, where he was preparing for the first space flight; in departmental museums of enterprises and scientific institutes that developed the first «Vostok» space rocket and the first «Vostok» spacecraft, where the first cosmonauts were trained for the flight; some items kept by the family of the First Cosmonaut, as well as private collectors. A large collection of items related to Yuri Gagarin are in museums that are not directly related to space and located in different parts of the country.

COMPUTER SYSTEM FOR STATOERGOMETRIC TESTING

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Introduction. One of the methods for diagnosing the physiological state of the organism of astronauts and predicting individual tolerance to large overloads is a functional statoergometric test, which determines the fitness of the ability to maintain static tension of the muscles of the lower half of the body in order to perform anti-overload techniques.

Purpose of the study. To develop an information-measuring system of statoergometric testing for automated analysis of its results both during the test and a posteriori.

Material and research methods. A training complex for statoergometric testing has been implemented according to the principle of control from a single terminal using auxiliary automation algorithms. For the information-measuring system of statoergometric testing, this principle is implemented through the use of a central processor, to which electronically controlled components of the training complex are connected via digital communication lines - a statoergometer, an electrocardiograph and a blood pressure meter. Information from these devices in real time is fed to the computer, processed, displayed on the display and saved to the database. Information processing algorithms are divided into five key groups: preparation, background recording of physiological indicators, retention of static loads, recovery after exercise, and the formation of a conclusion. The first classical program of statoergometric testing provides for sequential (without interruptions) holding five stages of static loads 120, 160, 200, 240, 280 kgf for 30 s for each stage of the load. The second classic program - four steps 120, 160, 200,

240 kgf, 30 s for each load step. Data registration takes place in a separate software process. In parallel, the processes of recording an electrocardiogram and measuring blood pressure are performed, which are repeated for each step of the load.

Results and discussion. Having the results of the algorithm for assessing the quality of load retention at the stage of generating the report, it becomes possible to form their assessment on a scale comparable to that of the cardiovascular system. Estimates can be generated separately for each stage and for the entire sample. As a result of approbation of the stated assessment method, it was shown that among those who performed the static-ergometric test for «excellent» according to the classical assessment system, using algorithms for assessing the quality of load retention, it was possible to single out a group of subjects requiring additional training to confidently maintain proper physical shape.

Findings. The developed information-measuring system of statoergometric testing provides the possibility of high-quality performance of a statoergometric test by one doctor by automating the control of the conditions for its conduct and ensuring processing in real time.

This work was supported by a grant from the President of the Russian Federation for state support of leading scientific schools of the Russian Federation (NSh-2553.2020.8).

SPACE TECHNOLOGIES IN THE NEUROREHABILITATION

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The introduction of the innovative medical technologies developed at the Institute of Biomedical Problems of the Russian Academy of Sciences, the Center for Aerospace Medicine, the Scientific Center of Neurology of the Russian Academy of Medical Sciences, is a priority area in the rehabilitation of neuro-orthopedic patients. For the treatment and rehabilitation of the patients in a hypokinesia state caused by motor system disorders, the impossibility of early mobilization due to cerebrovascular accident, the consequences of the injuries and surgical treatment of the brain diseases and spinal cord, the medical technology «plantar support load simulator Corvit is used. The activation of the support afferentation in the physiological parameters of walking normalizes the ratio of excitation and inhibition processes in the central nervous system, helps to reduce stiffness, muscle spasticity, the development of functional connections in the brain, and improves the restoration of coordination of movements.

Since 2010, in the neurological hospital of the Central Clinic for Rehabilitation of the Federal Medical and Biological Agency of Russia, the technology of supporting afferentation stimulation using the Corvit apparatus has been included in the kinesitherapy for patients with severe motor deficits after injuries and diseases of the brain and spinal cord. 10004 procedures were performed in 1321 patients. 38 % of the patients had low rehabilitation potential due to the severity of the spinal cord and brain damage. According to the neurological status in 44 % of the patients had severe movement disorders in the form of coarse hemiparesis or hemiplegia, 38 % of the patients had lower paraparesis or paraplegia and 18 % – tetraparesis. The time from the onset of the disease ranged from 2 weeks to 60 months. The course of treatment for 10–18 days included daily procedures for 20–30 minutes, 1–2 times a day.

As a result of the treatment, a persistent improvement in the functional state of the neuromuscular apparatus was shown in all patients. According to the Bartell scale, data about the reliable positive dynamics of the increasing exercise tolerance, reducing the degree of paresis and spasticity were obtained. It should be noted that the procedure caused positive motivation in patients. No signs of lympho-venous insufficiency during training sessions on the Korvit simulator according to the developed programs were registered.

Thus, the developed methodological techniques for individual kinesitherapy programs using the plantar support load simulator Corvit significantly optimize the general rehabilitation program for patients with severe motor deficits, significantly increase the patient's motivation and improve the rehabilitation potential of patients.

PRELIMINARY RESULTS OF STUDYING THE HUMAN BODY PHYSIOLOGICAL ACTIVITIES IN SIMULATED MICROGRAVITY WITH REGULAR ARTIFICIAL GRAVITY SESSIONS ON A SHORT-ARM CENTRIFUGE

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Introduction. From the experience of medical monitoring space crews we know that microgravity challenges the human organism by deconditioning of the cardiovascular and muscular-skeletal systems, and induces hypohydration and hypovolemia. The countermeasures available on the ISS compensate these effects but partly for they cannot make up for the absent hydrostatic blood pressure, weight load of the muscles and bones, and altered functioning of the afferent systems. It appears

that artificial gravity (AG) produced by a short-arm centrifuge as an element of the space vehicle design will become a universal countermeasure. However, there are many issues that need to be cleared up through further testing of rotation protocols combining AG with simulated microgravity.

Purpose. Systemic studies of AG effects on various body systems of human subjects subjected to simulated microgravity (21-day dry immersion).

Methods. We performed 16 sessions with participation of two volunteers for short-arm centrifugation along the body axis (+Gz) at maximum 2.0 G at subject's foot. The total rotation time was 60 minutes and the plateau duration was 30 minutes. The rotation sessions were repeated after no less than two days in-between to guard against the cumulative effect and to check first the appearance and then maintenance of the favorable effect with each SAC session throughout 21-d DI.

During rotation we conducted continuous monitoring of participant's electrocardiogram (ECG), cuff blood pressure (BP), earlobe pressure (EP), time of motor response (MRT) to stimuli presented by device Perimeter, and continuous video feed by an experienced physician.

Results. Data analysis showed that tolerance of the +Gz values in the study was adequate, the recorded parameters responded regularly to centrifugation and never reached critical values; MRT duration was within the normal period. During the initial first three SAC sessions at the DI onset HR increased and EPs decreased. After that and till DI completion these parameters tended to stabilize fluctuating within their normal ranges.

Conclusions. Our results suggest that regular exposures to AG have a training effect on the cardiovascular system of the human in the condition of simulated microgravity. However, to strengthen this conclusion we will need to increase the number of tests.

FIBRO-ADIPOGENIC PROGENITOR CELLS FUNCTIONS ARE ALTERED DURING GRAVITATION UNLOADING

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Introduction. Skeletal muscle regeneration is a complex multistage process where different types of cells are involved. Whereas the main function of maintaining the regenerative potential is performed by satellite stem cells, fibro-adipogenic progenitors (FAPs) play an auxiliary role and provide trophic support to myogenic progenitors. FAPs are a muscle interstitial mesenchymal cell population, which supports muscle stem cells differentiation during tissue regeneration. However, in pathological situations FAPs promote fibrosis and fatty degeneration of skeletal muscle. But the exact mechanisms underlying the replacement of muscle tissue with adipose/fibrous tissue during these processes are still unknown. This study is aimed to reveal the FAPs functional properties during gravitation unloading.

Methods. We use hindlimb suspension (HS) model for simulation of gravitational (functional) unloading of the rat for one day. Then satellite cells and FAPs were isolated from soleus muscles of the rats according to the standard protocol. Adipogenic differentiation of FAPs was performed by replacement of proliferation culture media (10 % FBS, 1 % L-Glu, 1 % penicillin-streptomycin) with differentiation media (20 % FBS, 1 % L-Glu, 1 % penicillin-streptomycin, IBMX, Rosiglitazone and Insulin). We used real-time PCR analysis to evaluate dynamics of adipogenic differentiation, morphological and metabolic changes in control (non-differentiated fibroblasts) and adipocyte. mRNA samples were collected at 3 and 11 days after stimulation and without treatment. To assess the ability of FAPs to form adipocytes we analyzed: the main adipo-specified genes (*Fabp4, Atgl*), marker of FAPs (*PDGFRa*), mitochondrial gene (*Mfn1*), genes involved in maintaining energy balance (*Ucp2, PGC1a)*.

Results. Although we analyzed only one day of hindlimb suspension abnormalities in the adipo-differentiation mechanisms have already been identified. At first, we revealed a tendency towards a decrease in the mRNA level of marker of FAPs (*PDGFRa*) under gravitational unloading during all period of adipogenic differentiation. Secondly, reduced mRNA expression level of fatty acid binding protein 4 (*Fabp4*) in non-differentiated FAPs correlates with low Adipose triglyceride lipase (*Atgl*) mRNA level which indicates problems in lipolysis. Also, we have found some issue with genes involved in in maintaining energy metabolism (*PGC1a* and *Ucp2*). All these genes show decreased mRNA level under adipogenic differentiation in hindlimb suspension model. Low mRNA expression levels of mitochondrial gene Mfn1 correlates with previously reported results indicating problems in mitochondrial metabolism.

Conclusion. Despite the early period of hindlimb suspension, there are noticeable changes in energy metabolism and biogenesis of mitochondria in FAPs. Identification of the mechanisms underlying these changes requires further and more detailed study with an increase in the unloading timing.

Work was funded by Russian Science Foundation grant #20-75-10080.

EVALUATION AND ASSESSMENT OF HEMODYNAMIC REGULATION – INFLUENCES OF THE LEG POSITION DURING TILT TESTS ON LEFT VENTRICULAR STROKE VOLUME

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Purpose. Most tilting-experiments are conducted on a tilt table (TT) with the legs in a straight position. However, the seated position, usually taken during rocket launch, flight maneuvers or centrifugation might have a different influence on venous return and, hence, the pumping function of the heart. The aim of this experiment was to analyse the potential differences in cardiovascular responses between a TT test with the lower extremities equal to heart level, and a tilt seat (TS) test, with the legs elevated above heart level, in the supine, tilted position.

Methods. 12 healthy subjects (1 female, 24 ± 3 y, 22.2 ± 1.2 $kg \cdot m^{-2}$) were tested on a TT (legs straight) and a TS (knee and hip joints in 90°, legs above heart level). In each setting, participants were tilted three times for 60 s from 90° upright to the 0° supine position (tilt-down) and back up to 90° (tilt-up, 120 s). Heart rate (HR) was assessed using a CustoGuard ECG belt (Customed, Ottobrunn, Germany) and mean arterial blood pressure was recorded beat-to-beat using Finapres Nova (Finapres Medical, Amsterdam, NL). Applying the Modelflow Algorithm, left ventricular stroke volume (SV) was calculated. Data were interpolated to 1 s-intervals and the three tilting maneuvers were time-aligned and averaged for TT and TS, respectively for each participant. ANOVA with the factors 'LegPosition' (TT, TS), and 'Time' (60 s of tilt-down, 120 s of tilt-up, each in 1 s intervals) was used to calculate differences between TT and TS for HR and SV.

Results. Significant main effects for LegPosition*Time were found for SV ($p < 0.001$) and HR ($p < 0.001$). SV response was greater for TS during the first 10 s of the 90° phase (TS: 0° - 90°: 90–115 ml vs. TT: 90 – 100 ml; $p < 0.05$), but was similar during the tilt-down phase. HR response was increased more in TT (58 min^{-1}, 10 s after the tilt-down, 80 min^{-1} after 10 s of 90°) compared with TS (62 - 74 min^{-1} at the same time points; $p < 0.05$).

Discussion. Especially SV during the first 10 s of tilt-up during TS was much greater compared to TT. Since SV was similar during the tilt-down phase, some of the venous return must have been stored in the pulmonary venous system. The different cardiovascular responses, and most likely the load of the pulmonary venous vascular system, in the two leg-positions should be considered for the seating position in human centrifuge experiments as well as for space travelers during launch and re-entry. Additionally, the different responses to tilting using different leg positions should be considered for the assessment and evaluation of the cardiovascular regulation in patients. TS experiments provoke greater changes in SV, TT experiments induce greater responses in HR. This might trigger different cardiovascular responses, depending on the individual health condition.

THE ROLE OF A DOCTOR IN A LONG-DISTANCE SPACE FLIGHT

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The topic of the doctor's role in a long-distance space flight is becoming increasingly relevant in terms of the discussion of manned deep space exploration, since the conditions of such a flight impose different requirements on the system of medical and biological support. The main distinctive features of medical support in long-distance flights are:

– autonomy,
– restrictions (including minimizing the volume and weight) and the specificity of medical supplies and equipment,
– the inclusion of a doctor in the crew.

The experience of Russian doctors who took part in space flights as crew members shows that the presence of a doctor confers an undeniable advantage on the crew. The doctors' participation in space flights accompanied all qualitative changes and breakthroughs to new levels in Russian and Soviet manned cosmonautics, since it was necessary to assess the impact of newly appeared factors on the cosmonauts' bodies.

Obviously, an interplanetary space flight will require reviewing the entire system of crew medical support.

First of all, this would be a change in the requirements for the doctors' qualification and training. The crew doctor must have deep theoretical and practical training in the field of space medicine, be skilled in a variety of diagnosis and treatment methods, provide various medical care – surgical, therapeutic, dental, psychotherapeutic, be able to promptly neutralize problems caused by extreme situations and conditions, have the ability to explore new methods and solutions to problems not previously encountered in his/her practice. Also, the doctor will have to take on the aspects of post-flight rehabilitation in

the case of flights with landing on space objects. At the same time, specialists who have also been trained as engineers and pilots should have an advantage in the selection process, so that the inclusion of a doctor in the crew does not increase the functional load on other members.

In addition, the training of a helping specialist from crew members without medical education – a paramedic, as well as additional training of the support group in the Mission Control Center should be the mandatory stage of medical support in long-distance flights.

The inclusion of a doctor will allow the use of more advanced and specialized medical kits on board, and the autonomy of the flight will require additional on-board means of decision-making support and tools for performing procedures and manipulations. Given the high autonomy of the flight, a medical and biological laboratory should be set up on board, and the crew doctor should be fully aware of its equipment and functionality.

Thus, for a long-distance space flight, the inclusion of a doctor in the crew seems necessary, since only in this case can the health of the crew members be preserved to the maximum extent possible. At the same time, the protocols of medical training and medical support should be revised and expanded.

ARTIFICIAL INTELLIGENCE TECHNOLOGIES IN THE SYSTEM OF ACCOUNTING FOR THE CAPABILITIES AND ABILITIES OF COSMONAUTS

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The organization of systemic accounting of human capabilities and abilities in aviation and space is an achievement of national science. It is based on psychophysiological analysis of professional activity. The founder of the concept and methodology of such analysis was professor G.M. Zarakovskii. Taking into account the results of psychophysiological analysis of activities in the design, development and exploitation of aerospace equipment ensured the safety of flights at the world level. Artificial intelligence technologies contribute to the task of accounting for psychology, capabilities and abilities of human beings. The directions of use of these technologies in the development and exploitation of aerospace technology are the improving the theory of biomedical, psychology engineering and ergonomic research in aerospace, justification of requirements for means, organization and working conditions, psychophysiological optimization of algorithms of work and maintenance of performance and assessment of the quality of training as well as psychophysiological rehabilitation and correction of the functional status of the flight crews. The compilation of data from medical, socio-psychological and ergonomics for the development and exploitation of aerospace technology has shown that taking into account the capabilities and abilities of humans using artificial intelligence technologies can improve flight efficiency and flight safety. Taking into account knowledge about human capabilities in the design of aerospace technology can reduce ergonomic deficiencies by 50 % and reduce their elimination by 20 %. Optimizing the display of information and controls taking into account the psychophysiological capabilities of the pilot reduces the time of detection of failures and malfunctions in the operation of equipment by 20 % and increases the accuracy of the performance of aerobatic parameters by 25 %. Implementation of recommendations on the formation and maintenance of the functional status of flight crew and cosmonauts increases their performance by 15–20 % and reduces psychology and emotion tension in flight by 15 %. The recovery time after flights is reduced by 15%. Professional reliability and situational awareness of the pilot increases by 20–30 %, while the time of spatial orientation of the pilot is reduced by 20 %, and the number of erroneous actions by 50 %. Taking into account the human capabilities and abilities during training reduces the time of preparation for flights by 20–30 %. The quality of retraining for new equipment is increased by 30–40 %, and the readiness of the pilot to extreme situations by 20 %. The pilot's resistance to overload and hypoxia can be increased by 40%, the effectiveness of protection means by 25–30 %. Optimization of socio-psychological working conditions reduces morbidity by 10–15 %, disqualification for health reasons by 10% and prolongs professional longevity by 3.5–4 years. In general, the system of human capabilities and abilities accounting allows reducing number of aviation incidents by 30 %, and flight accidents by 15 %. The expected medical-technical, socio-psychological and ergonomic effect of taking into account the capabilities and abilities of humans using artificial intelligence technologies can reach 18–45 million rubles per 1 million rubles of expenditure per year.

ASTROBIOLOGICAL ASPECT OF THE RESISTANCE OF FUNGAL COMMUNITIES FROM DESERT SOILS TO THE IMPACT OF THE SIMULATED MARTIAN CONDITIONS

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The modeling of extraterrestrial environments is one of the ways for investigation the possibility of biological life form existence on different objects of the Solar system, for studying of the potential ways of microorganism adaptation and evolution under extreme conditions. It is informative to use the models which have parameters as close as possible to the conditions of astrobiological target objects. In this case the natural microbial communities of extreme habitats of the Earth, similar in a number of physical and chemical parameters with some of the planets and bodies of the Solar system can be the objects of study. Microbial communities of such habitats have the widest set of mechanisms of protection from the effects of stress factors. The aim of this study was to analyze the reaction of fungi communities from desert soils to the physical impact simulated long-term presence in extraterrestrial conditions. Samples from the upper humic horizon of grey soil (Negev desert, Israel) and grey-brown soil (Moroccan mountain desert) were the objects of the present research. The samples were irradiated by high doses of gamma-radiation (0,1 and 1 MGy) and accelerated electrons (0,05; 1; 2; 3; 4; 5 MGy) at low temperature and pressure in the climatic chamber. One part of the samples was affected only by temperature and pressure without any irradiation. For culturing of fungi the method of soil suspensions inoculation was applied using solid Czapek medium and alkaline agar. Soil suspensions were warmed before inoculation (52°C, 2 min). The fungi were cultivated at temperature 5 °C, 25 °C, 37 °C. The amount of fungal biomass in situ and its morphological structure were evaluated by the method of direct fluorescent microscopy with calcofluor white, ethidium bromide and acridine orange dyes. The exposure of the soil samples to 0,1 MGy gamma-radiation activated the fungal communities – the quantity of fungal propagules, the number of species and fungal biomass increased. Whereas the exposure to 1 MGy gamma-radiation led to the elimination of many species. The most resistant species which dominated after the impact of extreme conditions were Aspergillus fumigatus and A. niger.

The influence of low temperature and pressure had no significant effect on colony forming units (CFU). The impact of accelerated electrons activated the germination of species with small spores but the total biodiversity decreased. Many colonies of yeast were observed after the irradiation with accelerated electrons at a dose of 1 and 2 MGy. The obtained results testify to the possibility of prolonged survival of eukaryotic natural communities in conditions of Mars regolith, and also in the space environment inside of small bodies.

DIRECTIONS OF COMMERCIALIZATION OF MANNED SPACE EXPLORATION

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The paper discusses the possibility of commercialization of such an industry as manned space exploration, which has always been considered a purely public sector. For 60 years, since the launch of the first spacecraft, manned space programs have been the prerogative of the government; have been a symbol of national power and an instrument of national policy. However, at the beginning of the 21st century, the situation changed. Roskosmos began to carry out commercial flights to the Russian segment of the ISS. In 2012, SpaceX's first private commercial cargo spacecraft Dragon performed a flight to the ISS. Nowadays, private manned spaceships are being created and flying into space in full swing, the first private spaceport «America» has been built. Manned space exploration has become a sphere of interest for private companies and individuals. Today government agencies are borrowing some technologies and products created by «private traders». In the next 15–20 years, the space services market will split up, and the place of private companies on it will become quite significant.

EXPERIMENT TO STUDY THE IMPACT OF HYPOMAGNETIC FIELDS ON THE ORGANISM OF A PERSON «ARFA-19»

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In the light of the preparation of mankind for the exploration of deep space, the question makes presence about the absence of the Earth's magnetic field in the natural environment of the astronaut. At a distance from the Earth's magnetosphere, the

magnetic field will drop to 1,000–10,000 times. According to the literature review (Bingi, 2017) hypomagnetic conditions impact on the regulatory mechanisms of the superior nervous activity and the cardiovascular system, secondary influence on blood, metabolism, pain, and various systems and indicators of biological objects have been studied.

In 2019, in the Institute was organized and conducted an experiment with the name «Study of the impact of hypomagnetic conditions on the psychophysiology condition on the organism of a person in the acute period of action» (encryption – «Arfa-19»)

Objective of the study: the study of the impact on the simulated factor of the hypomagnetic atmosphere (On average it was achieved a reduction of 800 times the magnetic field), on cognitive, operator functions, auditory analyzer and indicators of pain sensitivity and cardio-respiratory system of the human obody under conditions of 8-hour exposure in a hypomagnetic environment.

The experiment was carried out with the participation of 8 male test subjects with a height of 185 cm and a weight of 90 kg, signed and informed voluntary consent, passed clinical selection (no acute and chronic diseases).

The installation of «ARFA» is a scientific medical and technical complex that, under ideal conditions, reduces the Earth's magnetic field to 1,000 times. The hypo magnetic conditions are created by compensation of the Earth's natural magnetic field by a ring system whose combined magnetic field vector is directed in the opposite direction of the geomagnetic field.

Design of the study: Randomized double-blind placebo controlled.

Conditions of the experiment: Fasting, the subject, in a sitting position, limited movement, with a single meal (lunch) equal to no more than 300 kcal during the experiment, environment temperature from 18–25 degrees.

The experiment was held with every test subject for 3 days. Every test subject took part in 3 experiments, respectively. The experiment schedule was designed so that there would be a pause of at least 7 days between repeated experiments (1, 2 and 3) for each subject.

Experiment 1 – adaptation-training day (ATD): A 4-hour training session in the installation to create magnetic fields «ARFA» without creating a hypomagnetic environment, to adapt the subject to the conditions, experimental techniques, hypokinesia, preliminary instruction and training in techniques requiring this was carried out.

Experiment 2 – hypomagnetic conditions (HC): an 8-hour exposure to a hypomagnetic environment in an installation to create magnetic fields «ARFA».

Experiment 3 – Placebo: 8-hour research in the installation to create magnetic fields «ARFA» without creating hypomagnetic atmosphere.

Experiment 2 (HC) and 3 (Placebo) were randomized.

The results of the experiment will be presented by the experimenters as an article and theses, the current publication is sent to awareness with the experiments.

STOCHASTIC AND SINGULAR ANALYSIS OF FRACTAL SIGNALS FOR SPACE BIOMEDICINE SYSTEMS

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Introduction. The report is devoted to the consideration of methods for the analysis of experimental data for medical monitoring systems in the conditions of space flight on orbital stations and in the conditions of cosmonaut training on Earth, the creation of stochastic components of expert systems for the processes of diagnosis and therapy. The methods are relevant for creating mathematical models of the mechanisms of functioning of human organs and systems with fractal stochastic properties, as well as for space gastroenterology and other branches of biomedicine.

Purpose of the study. The aim of the study is to develop new approaches to the study of random processes with fractal and chaotic properties.

Research methods. Identification methods are based on algorithms for solving inverse ill-posed problems, including identification of the distribution laws of random biomedical indicators and verification aspects of test problems. The identification of the desired characteristics of the probability density is performed by solving the Fredholm integral equation of the first kind on a limited sample. The solution of such problems is based on regularization methods.

The proposed scientific approach also allows us to obtain new results and conduct stochastic analysis on a variety of indicators of the human immune system.

The results of the research. The results of a study on stochastic and singular analysis of the experimental implementation of a fractal random process – the EGG signal (electrogastroenterographic signal) in gastroenterology (clinical data) are presented. Identified the distribution of local segments of the process based on the developed algorithms and programs for the diagnosis, implemented a modification of the singular spectral analysis (SSA method) in order to compress the signal and faster Troubleshooting; investigated the trajectory matrix EGG signal. It is shown that the segments of the EGG signal and their first differences (up to the third) have polymodal distribution densities [Kulikov V., Kulikov A., Ignatyev A., 2021)].

Conclusions. The identification time of a single polymodal distribution depends on its complexity and ranges from a few tenths to 10–15 seconds with a sample size of up to 10,000 samples, which allows us to consider the method as a rapid analysis. A similar diagnostic complex can be formed for the respiratory and cardiovascular systems.

The combination of SSA algorithms, wavelet analysis, the perturbation method, and independent components (ICA) will allow identifying dominant and latent factors in the study of the functioning of the gastrointestinal tract and other organs and systems of the astronaut.

The results of the performed studies are relevant for the data processing of the «Splanh» medical space experiment conducted by the SSC RF-IMBP RAS.

The research is carried out with the financial support of the Russian Foundation for Basic Research in the framework of scientific project No. 19-07-00926_a.

THE ROAD TO COSMONAUTICS OF MILITARY MEDIC IVAN AKANDINOVICH KOLOSOV

Kupriyanov V.N.

Ivan Kolosov was born in 1932. In 1957 he graduated from Military Medical Academy. After graduation from the Academy he was appointed for further service in the Polar Region. Pilots of the neighboring garrisons landed at them as a reserve airfield, when he performed duties of the chief doctor of the aviation regiment in the garrison of Kilp-Yavr on the Kola Peninsula.

One day a young pilot Yuri Gagarin was among them. It turned out later, when A. Kolosov was in Zvyozdny gorodok.

Serving in the North, Kolosov dreamed of scientific work in the field of medicine. But the reduction of the armed forces began. And he filed a report for dismissal. The commander of the unit, where he served, did not allow this report to go, and offered Kolosov to go to Moscow to the Central Research Institute of Aviation Hospital. It turns out that there was a request for him from the hospital, but at that time the regiment needed a military aviation doctor. When A. Kolosov was at the hospital there on business – checking his work – was Alexander Babiychuk, then FlagShip Doctor of the Air Force – Deputy Chief of the Main Military Medical Directorate of Soviet Army, who reported to Lieutenant General Philip Alexandrovich Agaltsov, Deputy Commander-in-Chief of Air Force for combat training (later – Marshal of Aviation). After a lengthy conversation between Babiychuk and Kolosov, he was assigned to a military unit which trained our cosmonauts.

The transfer order was signed on April 27, 1960. At first he was instructed to conduct training in pressure chamber, thermal chamber, surdochamber and during flights on airplanes reproducing short-term weightlessness modes.

During the first flight into space I.A. Kolosov was among the six physicians assigned to head teams who were included in the group of so-called «jumping» doctors who, if necessary, should have helped the astronaut when he landed in their area of responsibility. I.A. Kolosov with a group of his paratroopers was stationed at the airfield in Sverdlovsk (now Yekaterinburg). As is known, the flight ended safely. And the cosmonaut did not need the help of doctors, who were assigned to the route of the flight.

Until May 1976 I.A. Kolosov had served at Gagarin Cosmonaut Training Center at Zvezdny in the capacity of assistant to lead doctor, leading doctor and head of the Flight and Space Training Laboratory. He specialized in flights with cosmonauts in zero-gravity conditions. The total time of staying in weightlessness conditions during his years of work amounted to many hours.

After completing his service in the GCTC Kolosov continued his service at Kirov Military Medical Academy, doing teaching and research work at the department of aviation and space medicine. He has authored more than 156 scientific papers and co-authored a the book about on aviation and space medicine and the textbook «Space Medicine».

In 2011 the book by Kolosov «Pioneers of Russian Manned Cosmonautics: Memoirs of a Doctor of the First Squad of Cosmonauts of Russian State Research and Test Centre for Cosmonaut Training after Yuri Gagarin» was published.

Despite his deserved age, professor I.A. Kolosov, Honored Worker of Higher Education of the Russian Federation, continues to work at the Academy, passing his experience and knowledge to young employees.

In 2020 by the Decree of the President of the Russian Federation Ivan A. Kolosov, Professor of Aviation and Space Medicine Department, was awarded the Order of Honour for high personal performance and many years of conscientious work.

THE RESULTS OF BIOMEDICAL RESEARCH ON BOARD OF THE ISS AND ON EARTH – A CONTRIBUTION TO THE MEDICAL SUPPORT OF ORBITAL AND AUTONOMOUS FLIGHTS

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Throughout the operational period of the Russian segment of the International Space Station, a large amount of scientific and applied research were performed and unique results were obtained needed to improve medical provision of orbital and

long-distance flights. It is obvious that the main area of implementation of research results is the improvement of medical support for the health and performance of astronauts in-flight and after returning to Earth.

First of all, such developments include methods and tools for diagnostics of the health status of astronauts, aimed at predicting and early detection of various pathological conditions caused by prolonged exposure to space flight factors. A number of methods and devices have been developed to assess the space flights' negative impact on the musculoskeletal, cardiovascular, sensory and other systems of astronauts' bodies. The developments in the field of prevention of the negative impact of space flight factors are being constantly improved.

An important area of work of the Institute's specialists is the creation of life support systems for long-term space flights, including biological life support systems.

A number of the Institute's developments are based on studying radiation impact on living organisms and protection against it, as well as the hypomagnetic environment, which can be a significant factor limiting the exploration of deep space.

In addition to biomedical support of the ongoing orbital space flights, space biology and medicine specialists have to prepare the biomedical basis needed for realizing interplanetary manned missions and operating planetary bases. An integral element for conducting research on the influence of long-term, including interplanetary, space flight factors, and developing a system for preventing the negative effects of these factors is the construction of ground-based model experimental facilities. The Institute has broad experience in creating and operating such facilities, like the ground-based experimental facility for modeling long-term space flights, including Mars missions, the immersion bath for studying the effects of weightlessness and the short-radius centrifuge for research related to the development of means and methods of biomedical support for long-term interplanetary flights and planetary bases.

Thus, based on a large number of studies of human health and performance in extreme conditions of space flight related to the prevention of adverse effects on the human body, a whole range of methods and tools useful in space medicine have been developed. In 2002–2020, 138 intellectual property protection documents were issued, including 96 patents for inventions, 28 patents for utility models, 5 computer programs, 5 trademarks and 4 databases.

One of the quality indicators of scientific developments that have the prospect of practical implementation is the recognition of such developments at professional exhibitions and salons. From 2002 to 2020, the Institute has taken part in 117 exhibitions. Of these, 73 were in Russia and 44 were abroad.

Participation in exhibition activities provides an opportunity for further use of space medicine achievements in social and economic spheres, as well as ensures their popularization and the creation of a positive image of the organization.

DYNAMICS OF HEARING MASKING THRESHOLDS IN A 4-MONTH EXPERIMENT WITH ISOLATION «SIRIUS-18/19»

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During space flights, as a result of constant exposure to noise, the levels of which exceed the permissible values according to GOST R 50804-95 and SSP 50094, dysfunctions of the auditory analyzer develop, which manifests itself in an increase in hearing thresholds.

In occupational health, various research methods are used to determine the violation of the functional state of the auditory analyzer, including the definition of hearing masking thresholds.

The aim of the study was to study the state of hearing masking thresholds in the a 4-month experiment with isolation.

The object of research was the thresholds for masking hearing. The study and assessment of hearing masking thresholds was carried out before, during and after using a clinical audiometer AD229, a study of the subjective assessment of hearing and acoustic environment based on questionnaires, measurement of levels noise in all places where the testers stay with a precision acoustic analyzer from Brüel & Kjr type 2260.

Results:

– During isolation, the testers had a slight subjective hearing loss, a feeling of stuffiness in the ears and nose. Some testers noted some subjective worsening of hearing after coming out of isolation, which passed after a few days.

– According to the subjective assessment of the acoustic environment in the experiment, there were practically no comments and complaints about noise in the dynamics of the experiment from the testers. However, during the experiment, all of its participants identified sources of intermittent noise.

– In the inhabited compartments did not exceed the permissible values according to GOST R50804-95.

– Almost all of the testers to one degree or another showed an increase in hearing masking thresholds, both in the speech frequency range and at high frequencies at the 2nd month and by the end of the experiment by 1–13 dB. An increase in the thresholds for masking hearing at low frequencies could be associated with the masking effect of background noise from LSS (Life Support Systems).

– After the end of the experiment, not all testers showed a restoration of hearing masking thresholds, which was revealed in the dynamics of isolation. Particular attention was paid to the shift in hearing thresholds at frequencies of 4 kHz and 6 kHz.

– For 3 out of six testers, hearing masking thresholds did not recover at one of the frequencies (4 kHz or 6 kHz) by 7 days after the end of isolation, and for 2 out of six testers, hearing masking thresholds did not recover at least at one of the hygienically significant frequencies by 14 days after the end of isolation.

Conclusion. The results obtained showed that even low noise levels with prolonged and constant exposure can cause shifts in hearing masking thresholds due to the cumulative effect of noise exposure, which is the basis for the implementation of the most effective prevention methods.

THE EFFECT OF 4-MONTH ISOLATION IN A PRESSURIZED FACILITY ON THE PHENOTYPIC CHARACTERISTICS OF DENDRITIC CELLS OBTAINED FROM HUMAN PERIPHERAL BLOOD MONOCYTES

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In the course of 120-day isolation in a pressurized facility with an artificial habitat, an analysis of the phenotypic characteristics of dendritic cells (DCs), generated from peripheral blood monocytes of six test volunteers, was carried out.

Analysis of the phenotype of DCs transformed *in vitro* from peripheral blood monocytes of volunteer test-ers showed that in the background period, a common feature of monocyte differentiation in DCs is signs of DC immaturity, manifested by a high proportion of undifferentiated monocytes ($CD14^+$ $CD80^+$ and $CD14^+$ $CD86^+$ cells) and a low proportion of mature DCs ($CD14^-$ $CD80^+$ and $CD14^-CD86^+$ cells). However, already in the first period of the examination, during the stay of the crew members in the pressurized facility (on the 7th day of experimental exposure), a significant increase in the content of $CD14^-CD80^+$ and $CD14^-CD86^+$ cells and a decrease in the content of $CD14^+CD80^+$ and $CD14^+$ $CD86^+$ cells (table). In addition, it was found that the content of cells with the $CD14^-HLA^-DR^+$ phenotype in cell cultures was also significantly higher than in the background period. Subsequently, no signs of a decrease in the proportion of $CD14^-CD80^+$ and $CD14^-CD86^+$ cells were observed; on the contrary, on the 63rd and 120th days of the experimental period, an in-crease in the content of mature DCs was revealed, not only in comparison with the background level, but also relatively their content on the 7th day of the period of early adaptation to the conditions of isolation in the containment facility. It is important to note that on the 120th day of stay in the containment facility, all monocytes examined in 8-day culture of differentiation had an increased yield of cells with expression of CD83 receptors. However, on the 7th day of the recovery period, a clear tendency towards a decrease in the content of DCs with the expression of $CD80^-$, $CD86^-$, $CD83^-$, and $HLA\text{-}DR^-$ receptors in cell cultures was re-vealed.

The results of the conducted studies indicate an increase in the ability of the population of $CD14^+$ cells of peripheral blood to differentiate into mature DC expressing molecules necessary for the formation of an im-munological synapse and activation of T-lymphocytes (CD80, CD86, CD83, HLA-DR), under conditions of long-term human stay in a closed space with a modified environment.

The study is supported by the basic topic of the SSC RF-IMBP RAS (65.1.).

FIBRINOLYTIC SYSTEM STATUS AFTER SPACE FLIGHTS

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Introduction. It is known that after space flights, crew members experience subcutaneous hemorrhages of various nature and localization. According to the results of previous studies, after space flights there is an increase of the coagulation cascade internal path potential [Kuzichkin D.S., et al. 2010]. It is known that the increased formation of plasmin as a result of the intensification of fibrinolysis can promote the activation of factor XII, thereby accelerating the process of coagulation along the internal pathway [Sinkov S.V., Zabolotskikh I.B., 2017].

The aim of this work was to study the state of the human fibrinolytic system after the completion of space flights.

Materials and methods. We examined 27 male cosmonauts aged 37 to 60 years. The sample of cosmonauts was divided into three subgroups according to the nature of the subcutaneous hemorrhages observed after the flight: the 1st group – without visible hemorrhages, the 2nd - with petechial hemorrhages, the 3rd - with ecchymosis.

Venous blood sampling was carried out in the background period 30–45 days before the launch, as well as on the first and seventh days after the completion of the flight. In the citrated plasma of astronauts, the concentrations of plasminogen (PG) and D-dimer (DD), α-2-antiplasmin (AP) were determined by immunological and chromogenic methods on an automatic

coagulometer Sysmex CA-1500. Fibrinolytic activity (FBA) was measured by the XII-a dependent euglobulin lysis method. The statistical analysis was held using Wilcoxon and Mann – Whitney tests.

Results and discussion. In the background period, the values of all the studied parameters of the fibrinolytic system were within the reference values.

The concentration of PG was statistically significantly reduced ($p < 0.05$) both on the first and on the seventh days of the postflight period. Perhaps this was due to the consumption of PG during the activation of fibrinolysis. In addition, there was a tendency towards a decrease in AP activity. However, fibrinolytic activity and DD level did not change statistically significantly. Only in the third subgroup of cosmonauts, in whom subcutaneous ecchymosis was observed, the values of DD on the 7th day after the flight were statistically significantly higher than in the first group.

A decrease in PG concentration after prolonged flights may be caused by a decrease in the level of its synthesis. It should be noted that after short-term flights there was no decrease in the concentration of hemostasis factors [Kuzichkin D.S., et al, 2009]. It is possible the duration of space flights can largely determine the intensity of protein synthesis processes [Grigoriev A.I., et al., 1992].

Conclusion. Thus, in the absence of vascular damage after exposure to space flight factors, no pronounced activation of fibrinolysis is observed. In case of damage to blood vessels at the final stages of space flight, activation of fibrinolysis is noted on the seventh day of the recovery period, which indicates the activation of fibrin formation on the first day after landing.

Apparently, changes in fibrinolysis parameters after flights are of a compensatory nature, preventing the imbalance of procoagulant and fibrinolytic activity.

THE IMPACT OF LONG-DURATION SPACEFLIGHT ON THE HORIZONTAL VESTIBULO-OCULAR REFLEX (HVOR)

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Introduction. The Semi-Circular Canals (SCCs) and the Otoliths are the two main organs of the vestibular system responsible for balance and gaze-stabilization. Weightlessness impacts the otolith organs, the main gravity detectors, which is evident from the decreased otolith-mediated ocular counter roll reflex observed after spaceflight (Hallgren et al., 2016). However, as the SCCs are not gravity-dependent, it is expected that a prolonged stay in microgravity would not affect the vestibulo-ocular reflex (VOR) generated by the SCCs. But little is known about the intricate interplay between the otoliths and the canals. Despite the number of studies that have tried to reveal the effect of microgravity on the SCCs through VOR measurements in the past decades, most of those studies were strongly limited by a restricted sample size and short-duration missions (Clement et al., 2019; Reschke et al., 2018). This study aims to characterize the hVOR changes before and after a long duration spaceflight (>6 months) in an unprecedently large cohort of 44 pre- and post-flight vestibular measurements in cosmonauts.

Material and methods. 44 pre- and post-flight measurements were performed, of which 13 were from first time flyers (1F group) and 31 were from frequent flyers (FF, N = 31), by exposing cosmonauts to off-axis centrifugation before and after their 6-month space mission to the ISS. This study was conducted between ISS expedition 16 (2007) and ISS expedition 61 (2020). Measurements were done approximately two months preflight, three days after landing (Early postflight R+3) and nine days after landing (Late postflight R+9). The hVOR induced by the Visual and Vestibular Investigation System (VVIS) mini centrifuge was assessed and recorded with infrared googles during a 30-second acceleration phase until the maximum velocity of 254°/s was reached. Extraction of nystagmi and associated computations of Slow-Phase Velocity (SPV) and Time Constant (Tc) were made using a custom MatLab routine. The Time Constant of hVOR was then further statistically analyzed in SPSS (V.27), using a linear mixed-model with $p < 0.05$ as significance threshold.

Results. We found a significant decrease in hVOR time constant Early postflight (R+3) and Late postflight (R+9) compared to preflight ($p < 0.001$). A partial but incomplete recovery was seen nine days after the return of the cosmonauts (Late postflight R+9).

Conclusion. For the first time, our large sample size allowed us to reveal a significant effect of spaceflight on the hVOR. The time constant values measured in cosmonauts are in the physiological range. These findings show an interaction between the otoliths and the canals. Our hypothesis is that the effect shown after spaceflight on both the otolith and the canals are centrally mediated rather than peripheral.

SLEEP AND AUTONOMIC NERVOUS SYSTEM DURING A 4-MONTHS ISOLATION EXPERIMENT

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Introduction. Short sleep and sleep alterations are highly prevalent due to irregular work shifts and extreme working conditions. Impaired sleep negatively affects sleep quality, cognitive performance, and the regeneration of the autonomic nervous system (ANS), leading to autonomic stress, morbidity and mortality. A special group with a high sleep deficiency are astronauts due to strenuous physical and mental workload and extreme exogenous conditions that cause a dysregulation of the circadian rhythm and sleep-wake cycle in outer space. A cooperation IMBP with ICSM was formed to identify a way to predict performance ability of astronauts after impaired sleep. As part of the MANSA project (Modulation of cardiac autonomous nervous system activity by a simulated 4-month outer space transit-phase mission), we aimed to identify non-invasive biomarkers of the ANS that capture the effects of impaired sleep.

Methods. During our pilot study (ANSISS), a study protocol to measure ANS parameters with the Somnotouch RESP was developed, the smallest and lightest portable non-invasive polygraphy system currently available and employable in space. Now, the protocol and the Somnotouch RESP were implemented during a four months isolation experiment of SIRIUS-19, simulating an outer space transit phase mission. A within-subject design was applied with the six participants (3 men/ 3 women, age 34 ± 6 years). They were recorded at eight timepoints experiencing different sleeping conditions: 1x pre-mission and 1x post-mission (undisturbed sleep), 1x post-mission (undisturbed sleep), 6x during mission with undisturbed sleep (3x), complete sleep deprivation (1x), low sleep fragmentation (1x with waking up once for one hour), and high sleep fragmentation (1x with waking up five short times). ANS parameters were recorded with the Somnotouch RESP and sleep with a 1-channel EEG electrode attached to the forehead and sleep questionnaires.

Results. Subjective sleep data indicated subjects were most tired after sleep impaired nights, especially the night without sleep. Objective sleep data showed significantly reduced sleep efficiency during sleep impaired nights ($p < 0.01$) with a mean sleep efficiency of 65 ± 17 % during high sleep fragmentation and 77 ± 6 % during low sleep fragmentation. The LF/HF (low-to-high frequency spectral power ratio) - a parameter of the heart rate variability - was significantly increased during the night without sleep ($p < 0.001$, mean LF/HF=2.27 ± 0.7) while the other nights did not significantly differ (mean LF/HF range: minimum=1.31±0.4; maximum=1.85±0.4). Preliminary sleep stage data of mean heart rate, pulse rate and LF/HF showed a normal progression during the night with being lowest during deep sleep and an increase during REM sleep (dream sleep) for all nights, including the nights with sleep impairment.

Conclusion. The results reveal the strongest effects for the night with complete sleep deprivation. The increase of the LF/HF ratio indicates a lack of ANS regeneration. Heart rate variability parameters recorded with the Somnotouch RESP may be suitable ANS biomarkers to capture effects of impaired sleep parameter. However, the results also revealed that the subjects' ANS was in general quite robust towards subjectively and objectively impaired sleep. Further analyses are currently being conducted.

ASSESSING AND COMPARING EFFECTS OF SLEEP RESTRICTION AND SLEEP FRAGMENTATION ON THE AUTONOMIC NERVOUS SYSTEM – A PILOT STUDY (ANSISS)

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Introduction: Impaired sleep is highly prevalent, especially due to irregular work shifts and extreme working conditions (e.g. astronauts). It affects the regeneration of the autonomic nervous system (ANS) and cognitive performance ability. A cooperation with the IBMP (Russian Institute of Biomedical Problems) was formed to identify a way to predict performance ability of astronauts after impaired sleep. As part of the pilot project ANSISS (Autonomous Nervous System in Sleep and Space), we aimed to identify ANS biomarkers with a non-invasive portable recording system that capture the effects of impaired sleep.

Methods: A study protocol, assessing ANS parameters with a portable non-invasive polygraphy system, also practicable in space was developed. It was pilot tested under sleep laboratory conditions with two sleep alterations: sleep restriction (5 hours sleep and 3 hours wake bedtime) and sleep fragmentation (8 hours sleep, light on every hour). Twenty healthy male

participants (40 ± 7 years, BMI: 25 ± 2 kg/m^3) underwent both sleep interventions in a randomized cross-over design with a washout phase of 10 days in between. Each sleep intervention consisted of four nights: a baseline night followed by the intervention night and two undisturbed recovery nights. ANS parameters were recorded with the portable polygraphy system Somnotouch RESP. Additionally, a full polysomnography, a psychomotor vigilance task, and questionnaires on well-being and sleep efficiency were completed.

Results: Subjective and objective measures revealed that sleep restriction had a stronger effect on the subjects than sleep fragmentation, especially regarding the need of regeneration. During the restriction night, ANS parameter showed a shift towards higher sympathetic activity and lower parasympathetic activity during sleep with a recovery effect after waking up. The SDNN (standard deviation of normal to normal to normal interval), a parameter of the heart rate variability, significantly decreased in the restriction night from bedtime (median SDNN: 64.5ms, IQR 40.4/74.7ms) till being woken up after 5 hours of sleep (58.4ms, 42.2/74.9ms), and subsequently increased during the remaining three hours wake bedtime (70.3ms, 49.8/129.6ms; $p < 0.01$). Light sleep stages were more affected than the REM or deep sleep stage.The sleep restriction also showed a compensatory shift of the sleep phases (shorter sleep latencies, longer deep sleep phase, etc.), a tendency of a decrease in reaction time, subjective performance and subjective well-being with a subsequent recovery effect.

Conclusion: Our pilot study revealed that especially sleep restriction had a strong negative effect with a need for recovery. Identifying ANS parameter using simple sensory technology of electrocardiography to adequately assess effects of impaired sleep is critical especially during extreme challenges such as in the cosmos before going out in space. The SDNN parameter of the heart rate variability may just be a suitable ANS biomarker and may add to a new decision-making instrument as to whether or not an activity with high psychological / physical stress can be justified. Next, the study protocol will be applied during isolation experiments lasting several months and simulating a space mission.

60 YEARS OF MANNED FLIGHTS. FRANCE-USSR / RUSSIA COOPERATION IN THE MEDICO-BIOLOGICAL FIELD: THE SUCCESS STORY IN HUMAN SPACE FLIGHTS AND AUTOMATIC FLIGHTS

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France has started biological experiments with animals on sounding rockets (rats in 1961/1962, cats in 1963, monkeys in 1967). Franco-Soviet space cooperation began in June 1966. The joint medico-biological group was created in 1972 with Professor H. Planel from GRBS in Toulouse. It offers the Biobloc (Cosmos-782 in 1975) and Cytos (Soyuz-27 in 1978) biological experiments. In 1973, discussions began between Professor A. Bès from Toulouse and Ada Kotovskaya from the IMBP on the Minerve project (DS-1). In 1975, it was Professor L. Pourcelot's turn from Tours with the Doppler ultrasound (DS-2). Proposal from CNES to Intercosmos to put a French astronaut into orbit in September 1976 : the russian answer was positive in April 1979. Two pilots were selected in June 1980 and first manned flight happen in June 1982 (PVH mission). The flight program includes the medical experiments Minerve and Echographe, Posture of Professor A. Berthoz (Laboratory of neurosensory physiology of Paris), Cytos-2 and Biobloc-3. France and the USSR/Russia then carried out several cooperative manned flights: Aragatz missions in 1988, Antares in 1992, Altaïr in 1993, Cassiopeia in 1996, Pegasus in 1998, Perseus in 1999, Andromeda in 2001. In automatic flights, the two countries carried out experiments on Bion satellites from 1975 and Photon satellites from 1995 (IBIS). Today, cooperation continues in the international orbital station (ISS) with the CardioMed experiment, aboard the Bion-M biosatellites (MTB-2 experiment on Bion-M2 planned for 2023), as well as ground simulation within the framework of the SIRIUS-20/21 experiment (six people for 240 days) scheduled to begin in May 2021.

MATHEMATICAL PREDICTION OF GAS RELEASE FROM POLYMERS USED ONBOARD THE MANNED SPACECRAFTS

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Evolution of Volatile Organic Compounds (VOC) from polymeric materials (PMs) in the operation of manned spacecrafts and concentrations of VOCs migrating from the PMs are the factors affecting the health and performance of the crew. Also, it has a negative impact on the operational characteristics of the structures and equipment of the modules. Therefore, properly selected PMs with a priority of materials having minimum release of harmful chemicals will allow to maintain the level of air pollution onboard a spacecraft in accordance with hygienic standards which ensure the acceptable air quality for breathing during a spaceflight.

Due to the weight limit set up for the brand-new habitable modules, designed to long-term orbital and interplanetary missions, the total mass of the PMs could be increased from 20 to 50 %. The huge number of PMs (the main source of air

pollutants onboard the spacecraft) will be accompanied by an increase in the total pollution (∑total) of the air during a mission.

In this regard, the development of mathematical models, based on the initial off gas test (OGT) results from the PMs is a solution of the problem that allows to predict destructive changes in the PMs during a long-term operation without conducting of accelerated climatic tests. Also, the model will allow to assess the contribution to the total air pollution for each material and to carry out the air quality control for human breathing.

The VOCs releasing from 706 PMs have been analyzed under nominal (40°C) operating conditions on the Russian Segment of the International Space Station (ISS) as well as the gas release dynamics for 42 PMs during accelerated climatic tests (ACTs). The VOCs have been identified by gas chromatography with mass spectrometric detection and high-performance liquid chromatography.

The PMs, selected for ACTs, have been presented by all major types used onboard the ISS -rubber, composite polymers, sealants, etc. The sample for the statistical analysis has included the most significant PMs, as they have used in the ISS in high saturation.

The mathematical model to predict total gas release from PMs is based on the statistical analysis of the tested materials, including the initial, 10-, 25- and 30-years OGT results for 42 selected PMs. Statistical analysis has been performed using the one-way analysis of variance (ANOVA).

The use of cluster analysis and computer algorithms of the Statistica StatSoft ver. 8 allowed to divide general list of PMs in two groups. The total gas release from the PMs of the first group corresponded to the developed mathematical model. On the other hand, the PMs from the second group have significantly different total gas release for different periods of simulated aging.

It is important to note that some PMs from the 2nd group had OGT results, relevant to the 25-years of aging, which contain VOCs indicating to the processes of PM matrix destruction (chlorine-containing compounds, furans, phthalates, amides, diene hydrocarbons).

SARCOLAB-3: CHANGES IN KNEE AND ANKLE TORQUE GENERATION DURING A SIX-MONTH SPACE FLIGHT MISSION

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Introduction. Space flight induces significant loss of skeletal muscle mass and function in response to mechanical unloading of the neuromusculoskeletal system. As the means to assess strength during flight has not routinely been available, most of the data used to formulate these hypotheses have come from post-flight assessments (relative to pre-flight values). Thus, the purpose of this study is to examine the effects of space flight on knee and ankle strength and neuromuscular activation during 6 months of spaceflight.

Methods. Four crewmembers were tested before flight and on board the International Space Station (ISS) after 8.9 ± 3.0, 49.1 ± 10.1 and 131.5 ± 27.7 days in-flight using the Muscle Atrophy Research and Exercise System (MARES). Voluntary isometric torque during maximal knee extension and flexion and ankle plantarflexion were examined. The knee was tested isometrically at 90, 60 and 45 degrees of flexion and isokinetically at 60, 120, 180, 240 and 300 degrees per second. The ankle plantarflexors were tested at 20, 10, 0 and -10 degrees for isometric testing and 30, 50, 100 and 150 degrees per second for isokinetic testing. Each angle and speed were tested in duplicate and the highest torque produced was used for analysis. Surface EMG was simultaneously measured during all tests. Root mean squared (RMS) EMG within a 500 ms window centered on the time of peak torque was identified, and ratios of EMG to peak torque (EMG/T) were calculated for each contraction.

Results. Peak knee extension and flexion strength declined immediately inflight from preflight or baseline values (extension – 24 % to – 36 % and flexion – 26 % to – 31 %) and both showed a gradual but not full recovery by the third inflight test session. Ankle plantarflexion strength was maintained at the first inflight session but declined at the second test session. There was a slight recovery prior to landing but deficits were 4–18 % as compared to baseline measures. Neuromuscular activation during flight as measured by EMG generally showed that greater muscle activation was needed to produce similar levels of torque for both the knee and ankle testing sessions.

Conclusions. Results suggest that space flight results in an immediate decline of peak torque production for both isometric and isokinetic knee extension and flexion while ankle plantarflexion is somewhat protected until midflight. Current in-flight countermeasures appear to trend towards functional restoration of knee extension while knee flexion remained relatively unchanged and ankle plantarflexion strength was mixed.

This space flight experiment, SarcoLab-3, was supported by NASA, ESA and Roscosmos.

DEVICE FOR MECHANICAL URINE COLLECTION IN WOMEN IN MICROGRAVITY AND CLINICAL USE

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Experiments with the use of «dry» immersion have been carried out since the 70s. They simulate the effect of weightlessness on human physiology and studied the processes of adaptation to it. The participants in these experiments were exclusively men, since women faced hygienic difficulties: the lack of funds allowing to pee without leaving the bath of «dry» immersion.

They tried to solve this problem by several already existing methods known in medical practice. For example, in a hospital setting, patients use bedside urine bags, catheters, gel bags like pads. However, under conditions of being in a «dry» immersion bath, each of these methods revealed their limitations, which did not allow their use.

In 2020, an apparatus that solves the problem of long-term stay of women in conditions of «dry» immersion was developed – «Universal portable device for mechanical urine collection in women» (patent RU 197 838 U1). This device made it possible to carry out the world's first «dry» immersion with the participation of women.

The design of the device makes it possible to use it not only in baths of «dry» immersion, but also to use it as a reusable portable compact toilet in other conditions: in experiments with limited space (isolation experiment, barocomplex) or with limited movement (when lying or sitting on the surface). This device can find its application in the field of manned space flights, as well as used by patients of medical clinics and centers.

On the basis of the Federal Scientific and Clinical Center of Reanimatology and Rehabilitation, in 2021, pilot testing of the device began. The preliminary results of testing the device by women have shown the high efficiency and demand for this development. Further use of the device by patients will optimize the design and make it more convenient for everyday use.

PRELIMINARY RESULTS OF A COMPARATIVE STUDY OF THE HUMAN PSYCHOPHYSIOLOGICAL STATE UNDER SIMULATED MICROGRAVITY WITHOUT COUNTERMEASURES AND WITH THE USE OF CENTRIFUGATION

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The development of the problem of creating an artificial gravity on board a spacecraft using a short-radius centrifuge (SRC) is an important part of the development of medical support for future interplanetary manned space flights.

The purpose of our research is to study the subjects' psychophysiological state in the process of their adaptation to microgravity conditions, as well as the influence of countermeasures associated with the creation of artificial gravity.

Two experiments with «dry» immersion of the same duration (21 days) were conducted: without the use of preventative measures and with the use of SRC rotations. Starting from the 2nd day, the rotation was implemented every 3 days. The magnitude of the head-pelvis overload was 2 Gz and lasted 30 min, the whole rotation – 1 hour.

The study of the subjects' psychophysiological state was carried out using acoustic speech analysis, psychological, cognitive and psychophysiological tests.

The additional impact of the centrifugation «smoothed out» the process of acute adaptation to the conditions of gravitational unloading in the first days of the experiment, but at the same time it can be considered as an independent stress factor. Rotation on the SRC stimulated the subjects, and this also had aftereffects, which throughout the experiment created short episodes of adaptation to acute stress factors: readaptation to «Earth» gravity (and support reaction) and acceleration in the centrifuge.

Significant differences were observed in the days when SRC rotation was implemented under «dry» immersion conditions and without this effect. There was an increase in the percentage of pauses in speech, and solution of simple mathematical equations took the subjects longer on the days of rotation.

Errors in mathematical counting correlated positively with increases in the median pitch frequency and the number of voice impulses, and negatively – with the percentage of pauses and shimmer in speech. These patterns can be described as

the state of the human operators, in which they speak quickly, with a large proportion of high tones of speech, making fewer pauses, and in this excited state they make more mistakes in activities that require conscious control.

These results are preliminary. However, the discovered patterns require further research in this direction.

This work was supported by a grant from the Russian Science Foundation No. 18-75-10086.

ASSESSMENT OF THE FEMALE OPERATORS' PSYCHOPHYSIOLOGICAL STATE UNDER SIMULATED MICROGRAVITATION USING ACOUSTIC SPEECH ANALYSIS

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In 2020, the Institute of Biomedical Problems RAS conducted the world's first «dry» immersion with female subjects. Similar experiments involving men have been conducted since the 70s, which allowed us to study in detail various hypokinetic disorders, to identify the stages of their development, to reveal the underlying mechanisms in male subjects.

6 female volunteers were in the conditions of «dry» immersion for 3 days, and during this time a number of space medicine studies were carried out.

The assessment of the operators' psychophysiological state is an important component of the medical support in the conditions of a long-term space flight. Automated analysis of operators' speech allows for continuous monitoring of the crew members' condition, without interfering with their regular activities and with minimal involvement of MCC specialists.

In dynamics, we studied the pitch frequency (mean and median), the volume of speech, the number of voice pulses and pauses in speech, the shimmer and jitter.

The experiment showed some differences between female and male subjects in the acute acute period of adaptation to microgravity conditions. The acute period of adaptation in women began earlier than in men, and ended faster. It should be noted that women's speech characteristics responded to stress differently than in men: the volume of speech changed more significantly, while not the pitch frequency. Also, the women's pitch frequency decreased due to stress, and did not increase sharply, as it was in men in similar conditions.

There were significant correlations between the acoustic characteristics of speech and the performance in cognitive and sensorimotor tasks. Both similar and opposite patterns in females and males were discovered. For example, with increases in volume and speed of speech, women and men make more mistakes in mathematical calculation and in coordination tasks. At the same time, with fewer pauses (less silent fragments) in speech, women solve tasks more quickly than men.

Also in this experiment, for the first time, the results of comparing the method of analyzing the speech acoustics with the indicators of the FaceReader software, which detects the subjects' emotions manifestations in their facial expressions, were obtained. Significant correlations between pauses in speech (positive) and voice pulses (negative) and emotion of fear and also neutral facial expression were found (increased shimmer also correlated with fear). This may indicate the «freeze» response. Similar reactions could be noted when comparing the FaceReader and the Spielbergers' STAI – when women were most anxious, their faces were less expressive.

The study was supported by the Ministry of Science and Higher Education of the Russian Federation under the agreement No. _075-1502020-919 from 16.11.2020 about the grant in the form of subsidy from the federal budget to provide government support for the creation and development of a worldclass research center «Pavlov Center for Integrative Physiology to Medicine, High-tech Healthcare and Stress Tolerance Technologies».

GRAVITY AND MASTOID EFFUSION

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Mastoid effusion can occur in patients admitted to intensive care units, particularly in those with prolonged stay. The condition has been identified as potential source of fever and sensory impairment.1 Recently, mastoid effusions have also been observed in astronauts returning from long-duration space missions.2 On Earth, most people spend more than half of the day in an upright position such that gravity redistributes fluid towards the dependent parts of the body. During spaceflight, however, weightlessness produces a continuous cephalad body fluid shift. Indeed, astronauts commonly experience face

swelling and nasal congestion among other signs and symptoms of cephalad fluid overload including optic disk edema. Possibly, lack of gravitational pull is sufficient to elicit mastoid effusion. Therefore, we determined whether prolonged -6° head down tilt bed-rest, which models weightlessness conditions in space3, reproduces mastoid effusion. Moreover, we assessed whether artificial gravity through centrifugation is protective.

The Artificial Gravity Bed-Rest study (AGBRESA), which was conducted in 2019 as joint project between NASA, ESA, and DLR in Cologne, Germany, tested the utility of artificial gravity as potential countermeasure during 60 days strict -6° head down tilt bed-rest in 24 healthy adults. Participants were distributed to three groups, one control group only exposed to bed-rest, one group exposed to continuous artificial gravity for 30 minutes/day during bed-rest, and a third group exposed to intermittent artificial gravity for six times 5 minutes with 3 minutes breaks during bed-rest. Artificial gravity was elicited through centrifugation on a short-arm human centrifuge with 1G at the center of mass. We assessed cranial magnetic resonance images for mastoid effusions one day before bed-rest, at day 14 and 52 of bed-rest, and three days after bed-rest.

While no participant exhibited mastoid effusions before bed-rest, six participants showed mastoid effusions at bed-rest day 14. On bed-rest day 52, 15 subjects showed mastoid effusions. Of those, three were in the intermittent centrifugation group, six in the continuous centrifugation group, and six in the control group. Seven subjects showed one-sided and eight bilateral mastoid effusions. Three subjects, one in each group, showed severe mastoid effusions (Likert-scale ≥4), with one having associated otitis media. There were no cases of mastoiditis.

The important finding of our study is that strict head-down bed-rest reproduces spaceflight-associated mastoid effusion. The finding suggests that mastoid effusion can result from gravity-related cephalad fluid overload in the absence of additional risk factors. The phenomenon may result in part from blocked fluid drainage due to mucosal swelling and consecutive Eustachian tube malfunction. Strict head-down bed-rest can now be applied for detailed studies regarding mechanisms mediating mastoid effusion. Moreover, potential countermeasures can be tested in a systematic fashion. Artificial gravity for 30 minutes per day was not sufficient to prevent mastoid effusion. Possibly, the centrifugal force acting on the head was too low and short-termed. Since mastoid effusion could interfere with sensory and vestibular function, might increase the risk of barotrauma, and predisposes to mastoiditis the issue deserves our attention for astronauts and bedridden patients alike.

DEVELOPING AUTONOMOUS MEDICAL CAPABILITIES FOR EXPLORATION SPACEFLIGHT

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Humanity is preparing to expand human space exploration beyond low Earth orbit (LEO) to the Moon and ultimately Mars. Human spaceflight operations on the International Space Station (ISS) have demonstrated the successful execution of in-mission, on-board medical operations in spaceflight. However, the current concept of ISS medical operations is based upon continuous ground support via real-time communications, the possibility of rapid evacuation, and frequent resupply. As the proximity to Earth decreases for exploration missions, the current paradigm of space medicine operations will need to become progressively Earth independent and more autonomous.

The Exploration Medical Capability Element of the NASA Human Research Program has been working for a number of years on medical capabilities that will be necessary to enable a space medicine operational paradigm shift. This presentation will highlight two critically important areas of this work: advanced computing technologies that can assist with on-board clinical decision support using crew health, medical, and performance data; and medical system capabilities to aid both medically-trained and non-medically trained exploration crewmembers to perform complex medical procedures with little to no real-time Earth communications.

AEROSPACE MEDICINE IN THE FIGHT AGAINST CORONAVIRUS INFECTION

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Anti-epidemic measures in response to the spread of new coronavirus infection are universally focused. This means mobilizing the forces and means of the medical service to localize the centers of its spread and to organize the treatment of patients and restore their functioning. The spread of a new coronavirus infection among the flight crew has its specificity and danger. Even a mild form of the disease with its consequences can affect the functional capabilities of the pilot's body and its performance in high-altitude flights and breathing under excessive pressure. All this requires special attention of aviation doctors to prevent the disease of the flight composition, the organization of surgical treatment in case of infection

and systemic recovery of psychophysiological reserves of the pilot's body in the process of rehabilitation. At one time, these issues were the subject of a special discipline «Organization and Tactics of the Medical Service», which was part of the program of training doctors for the Air Force at the Military Medical Academy by S.M. Kirov. The specifics of limiting the spread of infection, identifying cases and using various means, methods and technologies for preventing the disease were studied. Meanwhile, medicine is not limited to the memorization of symptoms, syndromes, clinical manifestations and laboratory indicators of the presence of a certain disease and appropriate methods, means, drugs and technologies of their treatment. First, this knowledge is far from well-established and not always complete and exhaustive enough. The arsenal of diagnostic methods, medical equipment, medicines is replenished... Life conditions are also changing: new toxins, allergens, viruses appear... It follows that the profession of a doctor involves constant development, professional development, retraining, new structuring of their knowledge and perceptions. Secondly, the diagnosis of the patient's disease and condition is the result of analysis and comparison of clinical manifestations, complaints, survey results and laboratory data. At the same time, it is important to determine the cause, to determine the factors, conditions and circumstances that contributed to the development of pathological processes in the body. Hence the need to study the history, living and working conditions, problems and difficulties, including adaptation to the new status. All this is an essential feature of the use of medical knowledge. The result is the formation of clinical thinking as a system of forming an idea of the causes, course and consequences of the disease and determining the optimal individual strategy and tactics of the treatment process and psychosomatic rehabilitation of the patient. Based on the results of the analysis and evaluation of the effectiveness of the confrontation of coronavirus infection, aerospace medicine specialists prepared the issue of the journal «Aviation Medicine, Psychology and Ergonomics».

REDUCED GLIAL SCARRING THROUGH HYPERGRAVITY EXPOSURE

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Neural regeneration following injuries to the central nervous system (CNS) in mammals is inhibited by several factors. One important mechanism preventing axon regrowth and thus the healing of a CNS injury is the formation of the glial scar. Key players in glial scar formation are reactive astrocytes that migrate into the region of the injury and produce an inhibitory extracellular environment, rich in chondroitin sulfate proteoglycans (CSPGs) and other signaling molecules. These, in turn, have an inhibiting effect on axon growth and even actively induce axon dystrophy, which has severe consequences for patients, e.g., loss of neuronal signaling and in some cases permanent paralysis. We could show that exposure to altered gravity has a direct effect on primary astrocytes and that hypergravity in particular might be a viable tool to reduce glial scarring.

We cultivated primary murine cortical astrocytes *in vitro* under hypergravity conditions at constant 2g for several days up to weeks by using the DLR Multi Sample Incubator Centrifuge and compared key cellular characteristics with 1g controls. To investigate cellular dynamics and migration speed under hypergravity, we employed our Hyperscope platform at DLR, a fully automated fluorescent live-cell imaging microscope installed on the envihab human short-arm centrifuge (SAHC).

On the one hand we could show that astrocyte spreading, a well-known effect of 2D cultures, is significantly reduced by about 20 % due to hypergravity (2g) exposure, while on the other hand cell proliferation is unchanged. The diminished spreading of astrocytes in combination with morphological alterations indicates an impact of altered gravity conditions on the cytoskeleton. Since cellular migration depends on a dynamically rearranging actin and tubulin cytoskeleton, we expected an impact of hypergravity on the migrational behavior of astrocytes. To test this hypothesis, we performed *in vitro* wound-healing assays (scratch-assays) on cells exposed to hypergravity enabling an assessment of the migrational behavior of astrocytes live for the first 24h and on fixed samples for longer durations. As a result, astrocyte migration was confirmed to be diminished by about 33 % during an initial phase followed by cell adaptation with a less substantial but prolonged diminished migration rate with about 10 % reduction of cell velocity. Thus, hypergravity represents a stimulus that inhibits astrocytic migration, which in case of a CNS injury might reduce glial scarring and therefore increase neural regeneration progression. Initial spreading after seeding of astrocytes in hypergravity was decreased by over 55 % after 5 hours, indicating a strong effect of hypergravity on cytoskeletal dynamics early in the exposure. Epifluorescence life-cell imaging employing LifeAct-GFP astrocytes on the Hyperscope platform showed no changes in the actin stress fibers under hypergravity but an increase of filopodia at the cell perimeter and a decrease in lamellipodium formation. Our further steps are the identification of the underlying mechanisms, e.g. cytoskeletal alterations to generate an advanced model of astrocyte responses to altered gravity.

RESEARCH OF COMPOSITE MATERIAL FOR IMPROVING PERSONAL PROTECTION MEANS UNDER GAMMA RADIATION

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When exploring interplanetary space, there are risks of exposure to cosmic rays (CR) of the crew and equipment of spacecraft (SC). High-energy protons and heavy CR ions create intense secondary radiation in the material of spacecraft structures and in the soil of planets and space bodies. Therefore, there is a real danger of overexposure of personnel in spacecraft and on the surface of planets. At INR RAS, together with AO PTS, research is being carried out to improve the means and methods of emergency radiation protection for firefighters to ensure the environmental cleanliness of nuclear power. These methods can be used to improve the radiation protective personal clothing for work in conditions of cosmic radiation on the surface of the planets of the solar system.

The aim of the work was to develop new methods for measuring and monitoring the radiation-protective properties (RPS) of composite materials to improve personal protective equipment in conditions of gamma and beta radiation.

Spectrometric and dosimetric methods have been developed for studying the OCD of a polymer composite material with metal microparticles using radionuclide sources of cobalt-57 and strontium-90. The measurement of the absorption coefficient of gamma radiation and the attenuation of beta radiation by the composite material were carried out using a gamma spectrometer based on a NaJ (Tl) scintillation detector and an MKS-01R radiometer.

A method for determining the elemental composition and uniformity of the distribution of the metal component in the composite material has been developed.

A measuring stand has been created for measuring and monitoring a broadband composite material sample in the automatic mode of the OCS. The stand allows in continuous mode to measure the attenuation coefficients of gamma radiation with an accuracy of 1 % when collecting statistics with an interval of 1 minute.

The measured absorption coefficient of gamma radiation with an energy of 122 keV and the attenuation of beta radiation by the lead-polymer composite material were 2.5 and 160, respectively.

EFFECTS OF THIGH-CUFFS ON BONE REMODELLING UNBALANCE INDUCED BY SHORT-TERM DRY IMMERSION AND THE ASSOCIATED METABOLIC MARKERS

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Dry-immersion (DI) model creates a state closer to weightlessness than head-down Bed Rest and challenges the bone remodelling activity more dramatically. No study has considered the impact of thigh-cuffs on the bone remodelling unbalance induced by simulated microgravity.

The aim of this study was to analyse the effects of thigh-cuffs on early events induced by dry immersion on bone remodelling and associated metabolism markers. Their vascular effects were recently published by Robin et al (2020).

Study. Eighteen male subjects divided into Control (DI) or Cuffs (DI-TC) group were submitted to a 5-days unloading conditions, as provided by the «Dry» immersion model. DI-TC group wore the thigh cuffs during the 5 days of DI during 8 to 10 hours/day. Fasting blood samples were collected daily, at baseline (BDC), after 1 day- (DI_{24h}), 2 days- (DI_{48h}) and 5 days- (DI_{120h}) immersion then after 48h following the return to loading upright conditions (R_{+48h}). Key markers of bone turnover were measured in serum : C-terminal telopeptides (CTx) and Tartrate-resistant acid phosphatase isoform 5b (Trap5b) for osteoclast activity; Procollagen type 1 amino- N-terminal propeptide (P1NP), Bone-specific Alkaline Phosphatase (bAP) for osteoblast activity; total intact osteocalcin (OC) and its carboxylated (Gla-OC) or undercarboxylated (Glu-OC) forms for bone remodelling; Periostin for osteocyte activity. Changes in phosphocalcic metabolism (Calcium, phosphorus and Parathyroid hormone), Visfatin, Insulin-like growth factor 1 (IGF1), lipocalin-2 and Irisin were also investigated.

Results. DI induced an increased bone resorption as shown by higher Trap5b levels by 7 % and 14 % at DI_{24h} and DI_{48h}, respectively. CTx levels were unchanged. Bone formation was also affected with lower P1NP (15 %) indicative of inhibition of collagen type I synthesis and higher bAP (15 %) suggesting an increased bone mineralization. This bone remodelling remained unbalanced throughout DI period. At DI_{120h}, OC and periostin levels decreased respectively by 15 and 18 % compared to BDC rates. Calcemia increased as early as DI_{24h} and reached a peak at DI_{48h}. This is followed by a 18 % decrease in PTH levels at DI_{120h}. Phosphatemia remained unchanged. Visfatin was very sensitive to DI conditions with levels 120 % higher at DI_{48h},

which were maintained until DI_{120h}. IGF1 levels gradually increased until they reached 8 % higher values at DI_{48h}. Lipocalin-2, a potential regulator of bone homeostasis, and Irisin were unchanged. The metabolic profiles of bone resorption and formation remained very similar between the two groups. Contrary to DI group, a lack of a significant decrease in periostin was observed in DI-TC group. Moreover, thigh-cuffs would appear to have at least partially prevented the visfatin production.

Conclusion. Our data confirmed the rapid bone cellular activities unbalance induced by a short-term DI conditions in human. The DI period of 5-days evidenced an adaptation peak reached at DI_{48h} then the maintenance of this new metabolic state until the end of DI. Furthermore, the dissociation between synthesis and mineralization markers highlighted the existence of two bone formation phases. Unfortunately, thigh-cuffs did not prevent significantly the DI-induced deleterious effects on bone cellular activities and/or energy metabolism.

IMPACT OF ISOLATION ON CREW PERFORMANCE DURING THE SIRIUS-19 CAMPAIGN

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In the last decades, the main space agencies have been focusing on human space exploration missions in future lunar bases and long duration space travel. To ensure the success of long-term space missions, the potentially negative impact of isolation on the crewmembers should be studied for safety and performance monitoring purposes. In thos project (TELEOP) this effect was investigated with regards to human-robot interaction, and more particularly during the remote control of a rover that collects samples on the surface exploration of the Moon.

Isolation implies living in narrow spaces with limited privacy and having very little contact with people from the outside; those conditions mostly characterize human space missions. In order to study its impact, several analog mission campaigns have been run, such as: MDRS-189 and MDRS-206 (Mars Desert Research Station – Utah desert), ARES III (Lunares Research Base, Poland) and SIRIUS-19 (Scientific International Research In a Unique terrestrial Station at the Institute of Bio-Medical Problems of Moscow (IBMP) in Russia). In order to progress towards a more global assessment of a confined operator's cognitive state, an innovative protocol has been designed to analyze subjective and objective measures regarding a professional task. This study evaluates the correlation between the participants' performance (execution time and accuracy) in a teleoperation task with their reported mood, motivation and their measured cardiac activity during a ground-based analog space mission.

The facility considered was the NEK at IBMP in Moscow, Russia, with six participants (3 females; Mean Age = 33,4, σ = 6,656; 2 Americans and 4 Russians) during 4 months. Over the period of confinement, they undertook seventeen teleoperation sessions. Training sessions were run before and after the mission. The participants filled shortened versions of the PANAS and the IMI questionnaires to assess their motivation and mood before the task.

Additionally, their cardiac activity was measured. The main results are significant Spearman correlations between the reported feeling of confinement and task completion time ($\rho = 0.375$, $p < 0.01$) and the reported feeling of confinement with the positive affect component of the mood ($\rho = -0.547$, $p =< 0.01$). In addition, a general decrease of motivation was observed along the mission with the exception of a booster created by the Moon landing phase. The outcomes showed a strict link of confinement and teleoperation performance. Thanks to this unique approach in studying the impact of confinement in such realistic environments, the TELEOP project allows to learn more about this unexplored field and consequently to better prepare for future missions to the Moon and beyond.

MATHEMATICAL MODELING OF THE REACTION OF THE PHYSIOLOGICAL SYSTEMS OF THE BODY TO THE CONDITIONS OF ARTIFICIAL GRAVITY DURING PREVENTIVE MEASURES OF THE ADVERSE EFFECTS OF WEIGHTLESSNESS

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Prolonged exposure to weightlessness causes a number of structural and functional changes, including changes in hemodynamics with the development of detrained cardiovascular system (CVS). To compensate for the adverse effects of weightlessness, the use of artificial gravity (IST) is promising. The currently available concept for creating an IST on board a spacecraft is the use of a short-radius centrifuge (CRT) to create short-term, but periodically repeated loads.

In most of the studies used a variety of modifiable parameters of rotation. These studies have repeatedly confirmed the feasibility of using a centrifuge to compensate for the adverse effects of weightlessness. However, the question of the modes of application of the CDR remains open.

At the first stage, it seems rational to develop an optimal mode of operation of a short-radius centrifuge, in which the adverse effects of weightlessness are leveled while maintaining the well-being of the subject during exposure. Selecting the optimal mode in conditions of repeated experiments will be very long and expensive. Therefore, to optimize research, it is advisable to use mathematical modeling methods. Mathematical modeling will allow us to identify the most important parameters of the object for research and to build a hypothesis of the influence of various characteristics of the rotation of the CDR on these parameters.

The aim of the work is to substantiate the optimal modes of using a short-radius centrifuge for the prevention of adverse effects of weightlessness using mathematical modeling of the reaction of the cardiovascular system of the body to changes in the parameters of the IST in the conditions of model experiments.

Methods of investigation. rheography and bioimpedance measurement (OCTOPUS-2); medical monitoring equipment: heart rate, ECG, blood pressure, respiratory rate, pressure in the earlobe; video monitoring; perimeter: medical control of the reaction rate, self-control of the tester; assessment of the CCC state before and after exposure to IST (ortho-test).

Conclusion. the work is planned to evaluate the influence of the variable parameters of the IST on the parameters of the cardiovascular system of the human body, to determine the degree of their variation and to give recommendations on the use of the most optimal rotation parameters.

APPROACHES TO THE ASSESSMENT OF CARDIOVASCULAR FUNCTIONALITY AT THE ISS

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The main features of the autonomic regulation of blood circulation in short-term space flights were described by Soviet scientists back in 60s of the last century. It happened immediately after the first manned flights into the space. More serious studies became possible with the creation of the Salyut and Mir orbital stations. It showed that during long term space flights there were significant changes in the circulatory system and the reconfiguration of the regulation system. It was found out that one of the main targets of the effect of microgravity is the cardiovascular system. Adaptation of hemodynamic due to regulatory mechanisms begins from the first hours of space flight and at different stages of a long stay in microgravity the level of heart functioning and regulatory processes is different. To quantify the adaptive effect, the parameters of heart rate variability can be used, because they reflect the activity of various parts of the regulatory mechanisms. For over than 50 years, HRV analysis has been used for research in space flights and in ground-based experiments. But so far it has not exhausted all of its capabilities and we continue to use it with additional methods to assess the status of all our crew members on board of the ISS.

Long-term researches, technology and techniques which were carried out by Russian scientists at the Salyut and MIR orbital stations have been modified and used or have being used for conducting scientific experiments at the International Space Station.

Space scientific experiments «Pulse», «Pneumocard» and «Cardiovector» have been carried out in cooperation with our foreign partners onboard the ISS since 2002 to the present time. They are constantly being improved and complement each other.

Data analysis of experiment «Cosmocard» consists of 24-hours of ECG monitoring with further analysis of ECG-signal electrical microalternations named ECG dispersion mapping.

Another large part of our research is related to the study of sleep quality. The «Sonocard» experiment was carried out by 22 Russian cosmonauts, and now a new space experiment is being prepared. It will make it possible to continue these studies at a modern level.

All these many years of research have given us a large amount of data from more than 50 cosmonauts that can be analyzed both individually and for statistical purposes for the understanding of processes of adaptation to microgravity.

Analogs of these devices were developed for the ground-based experiments and for medicine on the Earth. One of the main areas of the further development of technologies is creation of mobile system for pre-medical screening researches and prenosological estimations of risk of development of cardiovascular diseases not only in space cardiology but also for medicine and Earth healthcare and applied physiology.

ARTERIAL STIFFNESS ASSESSED BY ESTIMATED PULSE WAVE VELOCITY IS NOT AFFECTED DURING 6 MONTHS SPACEFLIGHT

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Background. Spaceflight challenges the cardiovascular system in manifold ways such as cephalic fluid shifting, space radiation and psychosocial influences. Vascular ultrasound measurements during space flight indicated an increased intima media thickness of the internal carotid artery. We have recently shown that estimated pulse wave velocity (ePWV) as a surrogate for vascular stiffness and therefore a measure of cardiovascular risk is not elevated after 6 month in space. We now present first inflight data based on monthly measurements in 4 cosmonauts.

Methods. After giving informed consent we conducted non-invasive hemodynamic assessment via upper arm oscillometric cuff approach (Mobil-o-Graph, IEM, Stolberg, Germany) in 4 cosmonauts undergoing 6 months space flight mission. We measured peripheral blood pressure, heart rate and central blood pressure. PWV was estimated (ePWV) from peripherally recorded pulse waves based on the wave reflection theory. Measurements were conducted twice before flight, every month during space flight, as well as on day 2–4 after return to earth. Baseline values were averaged. Results are reported as means±standard deviation. For longitudinal comparison ANOVA with repeated measurements was used.

Results. Subjects were male, age was 52 ± 3 years with a body-mass index of 27 ± 4 kg/m². Mean blood pressure before flight was 132 ± 16 / 84 ± 12 mmHg with a heart rate of 62 ± 4 bpm and an ePWV of 7. 6 ± 0.6 m/s. In the longitudinal analysis of repeated measurements blood pressure, heart rate and ePWV did not change significantly over the time course until return to earth despite a drop of diastolic blood pressure and slightly reduced ePWV at the end of spaceflight (123 ± 12 /75 ± 8 mmHg and 7.4 ± 0.1 m/s). Furthermore, we could not observe significant differences when comparing the last measurement after 6-months in space with values obtained before flight and after landing.

Conclusion. Neither after return nor during 6 months in microgravity we observed an increased cardiovascular risk of cosmonauts based on ePWV used as vascular biomarker. Instead blood pressure and ePWV tended to decrease during spaceflight. More direct measures of arterial vascular wall properties in a prospective manner may be needed to proof these findings.

HEMODYNAMIC REACTIONS FEATURES OF A FEMALE BODY IN CONDITIONS OF «DRY» IMMERSION

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First female volunteers were involved in an experiment of «dry» immersion conducted by IBMP at the end of 2020. 6 women (average age 30.2 ± 5.5) were selected by the Clinical department due to all requirements for such investigations. They all signed an experimental agreement approved by the Biomedical Ethics Commission of the SSC RF – IBMP RAS. The duration of exposure was 3 days. Measurements were carried out at the same time every day during exposure, as well as before and after immersion on the 2nd day at the end of the experiment.

In addition to the analysis of the electrocardiogram (heart rate variability and dispersion mapping of the myocardium), an important role is played by the assessment of the parameters of central hemodynamics and the possibility of assessing the early aging of blood vessels.

Medical devices that provide non-invasive measurement of parameters of central hemodynamics and vascular function are becoming increasingly important for predicting cardiovascular risk also in clinics. Laboratory-experimental and indirect research methods are used because direct determination of the elasticity and extensibility of living tissues is practically impossible. For this aim the «Mobilograph» device which certified for similar purposes in real space flights was used in the experiment with «dry» immersion.

The results of measurements of central aortic pressure, cardiac stroke volume, vascular resistance and pulse wave velocity allow to conclude that 3 days of immersion exposure did not lead to clinically significant changes in the indicators of early vascular aging. Obtained data allowed to judge about individual characteristics of cardiovascular system adaptation of 6 healthy subjects during the exposure of «dry» immersion. The mechanisms of regulation are similar to those that are detected of cosmonauts, but the changes are less pronounced, statistically unreliable and quickly reversible.

The research was carried out within the framework of the basic topics 63.1 and 64.1 of the Russian Academy of Sciences for 2013-2023.

THE CONTENT OF HORMONES AND MARKERS OF BONE METABOLISM IN THE BLOOD OF RATS AFTER 7-DAY ANTIORTHOSTATIC SUSPENSION WITH THE USE OF DENOSUMAB

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In the last decade, our understanding of the pathogenesis of bone and mineral disorders that occur under the space flight factors has increased significantly. However, the issues of drug prevention of the risk of osteoporosis and bone fractures during flights into deep space remain open. The use of denosumab (DS, a human monoclonal antibody to the ligand of the activator receptor of the nuclear factor κB) is one of the potential prophylactic approaches.

The purpose of this experiment was a comprehensive study of the mechanisms of bone tissue remodeling and experimental testing of DS as a means of preventing bone loss when the animal body is affected by simulated microgravity. One of the objectives of the experiment was to evaluate the effect of DS on the content of hormones and markers of bone metabolism in the blood of rats after 7-day antiorthostatic suspension.

Wistar line rats, which are traditional subjects for studying the effect of microgravity on bone tissue, were used in the first series of the experiments. Antiorthostatic suspension of rodents by the method of Ilin, Novikov (1980) modified by Morey-Holton (2002) was used as an experimental model. The experiment was approved by the Biomedicine Ethics Committee of the Institute of Biomedical Problems of the Russian Academy of Sciences / Physiology Section of the Russian Bioethics Committee Russian Federation National Commission for UNESCO (Minutes No. 529 dated November 12, 2019). Animals (32 males, weight 180 ± 20 g) were randomly divided into four groups with 8 rats in each: two groups of vivarium control (with and without denosumab; C+DS, and C, respectively) and two groups of suspended animals (hindlimb suspension with and without denosumab; HS+DS, and HS, respectively). Throughout the experiment, all animals had constant access to food and water. DS at a dose of 1 mg/kg was injected once subcutaneously before the launch of the experiment.

The concentration of ACTH, PTH, DKK1, FGF-23, Insulin, Leptin, Osteoprotegerin, Sclerostin were measured by multiplexed fluorescent bead-based immunoassay (MAGPIX, Luminex) according to the manufacturer's instructions, using a Milliplex MAP Rat Bone Panel 1. Statistical analysis of the data was performed using the Mann-Whitney U-test (the Benjamini-Hochberg procedure) in the STATISTICA 10 software.

At the end of the experiment, the leptin level in the HS+DS group of animals was significantly lower than in the C+DS group. There was no significant difference between the groups without DS. At the same time, the weight of animals from the HS and HS+DS groups was significantly lower than that of animals from the corresponding control groups, and the weight of animals from the C+DS group was higher than that of rats from group C.

Now, 7-day exposure may be said to be not enough to assess changes in bone metabolism. However, these changes in leptin levels suggest that DS may have a positive effect with longer exposure, since previously, the protective effect of leptin on bone tissue was shown, regardless of other indicators of bone metabolism (Ducy et al., 2000; Steppan et al., 2000; Burguera et al., 2001).

TRANSIENT ACTIVATION OF SLOW MYOSIN EXPRESSION AFTER 3 DAYS OF RAT HINDLIMB UNLOADING IS CAUSED BY CALCIUM IONS ACCUMULATION

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Under conditions of real and simulated gravitational unloading, we observe a shift in the myosin phenotype of skeletal muscles from slow type to fast. There is a hypothesis about the transient activation of calcium-dependent mechanisms that maintain the expression of the slow isoform of myosin heavy chains (MyHC) gene during the 2–3 days of gravitational unloading, when the decrease in the expression of this gene temporarily stops. This phenomenon is probably associated with the activation of calcineurin and calcium-calmodulin kinase II (CaMKII).

The aim of this work was to test the hypothesis of calcium-dependent reactivation of slow myosin expression.

We used nifedipine as an L-type calcium channel blocker that was given intraperitoneally. Male Wistar rats were divided into the following experimental groups 8 rats each: vivarium cage control (C); 3-day hindlimb unloading (3HS); 3-day hindlimb unloading along with nifedipine injection (3HS+Nif). Animals from C and 3HS groups were saline injected as placebo (daily throughout the experiment). After the experiment soleus muscle samples was isolated and frozen in liquid nitrogen. By RT-PCR method we analyzed the expression of *myh7* gene (MyHC I(β)). Nuclear Factor of Activated T Cells 1 (NFATc1) and histone deacetylase 4 (HDAC4) content in the nuclear fraction was analyzed by electrophoresis and Western blot.

After 3 days in 3HS group we observed no any changes in the *myh7* gene expression compared to C group, which is consistent with the earlier data. In 3HS+Nif group expression of *myh7* gene was significantly decreased as compared to

C group, which confirms the hypothesis of calcium-dependent reactivation of slow myosin expression, since nifedipine prevents the accumulation of calcium ions in the myoplasm. The content of NFATc1 in the nuclear fraction in groups C and 3HS did not differ, while in the 3HS+Nif group the content of NFATc1 in the nuclear fraction was significantly reduced twice as compared to 3HS group. However, the calcium-dependent reactivation of the expression of the slow isoform of MyHC can be carried out not only due to the reduction of nuclear NFATc1, but also due to the calcium-dependent import of HDAC4 by its phosphorylation by calcium-calmodulin kinase II. There were no significant differences of HDAC4 content in the nuclear fraction between groups C and 3HS. Nonetheless, in 3HS+Nif group we found that the content of HDAC4 increased significantly.

Thus, we confirmed the hypothesis about calcium-dependent reactivation of slow myosin expression and that CaMKII / HDAC4 and calcineurin/NFATc1 is involved in this reactivation.

This work was supported by RSF grant # 18-15-00107.

CHANGES IN MOTOR CONTROL DEPENDING ON THE LEVEL OF PHYSICAL PERFORMANCE IN SPACE FLIGHT

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Prolonged exposure to microgravity is known to cause motor control changes. The success of interplanetary mission will depend on the ability to perform different motor tasks on the surface of other celestial bodies. The ability to predict the efficiency of working operations performance on a variety of space objects is an important task in preparing for interplanetary missions. The goal of our study was to determine the effect of the physical performance level on motor control changes after long-duration space flight (LDSF).

Eleven russian cosmonauts that performed space mission with the duration of 115–196 days aboard the International Space Station (ISS) in 2015-2018 took part in the study. Evaluation of changes in the motor control system was carried out using test «stepping over an obstacle». The test results collected 60–30 days before the flight and on the 3rd day after landing were compared. During the test, the cosmonauts were to walk at a self-selected speed along an 8–10 m long flat walkway and step over obstacles with different (5–30 cm) height. Light-reflective markers were located on the toe (at the site of the head of the fifth metatarsal bone) and on the obstacle edges. The clearance between the obstacle and the toe was determined by the vertical displacement of the markers. Biomechanical characteristics of locomotion were recorded using «Videoanalyzer Biosoft 3D» hardware/software and «Videomotion-3D» program. Video recording was made using two digital cameras «Baumer» sampled at 90 Hz. Changes in toe-obstacle clearance after the space flight were analyzed. The evaluation of physical performance level in flight was carried out via MO-3 test. The test was carried out on BD-2 in passive mode of canvas movement and included the following five steps: 3 min of warm-up walking, 3 min of slow running, 3 min of running at a moderate speed, 1 min of running at a maximum speed, and 3 min of cooling-down walking. The physical performance capacity was assessed by the physiological cost of work (physiological cost index) calculated as heart rate (bpm) to the maximum running speed (km/h) ratio and axial load levels (% of body weight). A correlation was shown between physiological cost in the MO-3 test and the change in toe-obstacle clearance after space flight ($r = 0,74$, $p \leq 0,05$). The time to perform the «stepping over obstacle» test also correlate with physiological cost in the MO-3 test ($r = 0,69$, $p \leq 0,05$).

Thus, the physiological cost in the MO-3 test may be a prognostic criterion of motor task successful performance after LDSF. These results could be used for work planning on the surface of other space objects.

The study was supported by the Russian Academy of Sciences base funding 63.1.

REDUCED VAGAL MODULATIONS OF HEART RATE DURING OVERWINTERING IN ANTARCTICA

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Maggioni M.A., Merati G., Castiglioni P., Mendt S., Gunga H.-C., Stahn A.C. Reduced vagal modulations of heart rate during overwintering in Antarctica Sci Rep. 2020 Dec 11;10(1):21810. doi: 10.1038/s41598-020-78722-3.

Long-duration Antarctic expeditions are characterized by isolation, confinement, and extreme environments. Here we describe the time course of cardiac autonomic modulation assessed by heart rate variability (HRV) during 14-month

expeditions at the German Neumayer III station in Antarctica. Heart rate recordings were acquired in supine position in the morning at rest once before the expedition (baseline) and monthly during the expedition from February to October. The total set comprised twenty-five healthy crewmembers (n = 15 men, 38 ± 6 yrs, n = 10 women, 32 ± 6 yrs, mean ± SD). High frequency (HF) power and the ratio of low to high frequency power (LF/HF) were used as indices of vagal modulation and sympathovagal balance. HF power adjusted for baseline differences decreased significantly during the expedition, indicating a gradual reduction in vagal tone.

LF/HF powers ratio progressively shifted toward a sympathetic predominance reaching statistical significance in the final trimester (August to October) relative to the first trimester (February to April). This effect was particularly pronounced in women. The depression of cardio-vagal tone and the shift toward a sympathetic predominance observed throughout the overwintering suggest a long-term cardiac autonomic modulation in response to isolation and confinement during Antarctic overwintering.

This investigation was supported by the ELIPS 3 and 4 programs of ESA and DLR grants 50WB0724, 50WB1030, 50WB1330, 50WB1525, and 50WB1915. We thank the crews who participated in the study and the Alfred-Wegener-Institut, Helmholtz-Zentrum für Polar- und Meeresforschung.

PROLONGED EXPOSURE TO CHRONIC INTERMITTENT HYPOXIA: EFFECTS ON CARDIAC AUTONOMIC MODULATION DURING SLEEP

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Hypobaric hypoxia is a potential adverse condition associated to spaceflights and extra vehicular activity and will get even more important in habits on Moon and Mars, in future. On Earth, high altitude is an optimal setting to study human adaptation processes to hypobaric hypoxia. In this view, a very interesting physiological model to investigate human adaptation to hypoxia is represented by the so-called Chronic Intermitted Hypoxia (CIH), which represents a unique condition were humans, over years, are repetitively exposed to hypobaric hypoxia, but for intermittent limited period of time only and not continuously. Indeed, intermittent hypoxia has been shown to enhance sympatho-respiratory coupling in rats and various studies have found correlation between intermittent hypoxia, autonomic disbalance and hypertension.

Miners in the Andes, and specifically in Chile, represent a unique category of lowlanders who, due to their work shift schedule (i.e., 7-day, 12 hours/day work at 4500 m asl, and 7-day rest at sea level), undergo the unique type of exposure to hypobaric hypoxia known as CIH. We investigated nocturnal cardiac autonomic modulation, by means of heart rate variability (HRV) analysis, in a group of 38 Chilean men miners, by recording 1-lead electrocardiography (ECG) continuously for 36 hours upon arrival at 4500 m asl, for the week of work. Subjects' characteristics, medical history, medication and exposure to high altitude were recorded.

Participants aged 48 ± 7 years, were overweight (BMI 28.9 ± 3), CIH exposure was 108 ± 64 months (mean ±SD) and fifteen of them were hypertensive. A window of 4-hour sleep during the first night in altitude was selected for HRV analysis. Despite no differences in ECG derived respiration and mean heart rate, we observed a substantial vagal depression in hypertensive subjects in comparison to non-hypertensive individuals. Further studies are needed to better elucidate mechanisms beyond this impaired adaptation, which might have an important impact on humans in future space missions.

This is investigation was supported by CONICYT / FONDECYT INICIACIÓN / 11180503/(Chile).

CARDIOVASCULAR AND AUTONOMIC EFFECTS OF NUTRITIONAL SUPPLEMENTATION DURING LONG-TERM BED REST

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Long term bed rest (LTBR) studies are a well-established analogue for spaceflights, specifically referring to the cardiovascular system. As part of the LTBR European Space Agency sponsored study entitled «Effects of a Nutritional Cocktail Consisting of Antioxidant and Anti-inflammatory Supplements to Prevent the Deconditioning Induced by 60 Days of Antiorthostatic Bed Rest», we evaluated the time course of cardiovascular parameters and cardiac autonomic modulation in 20 healthy male volunteers (TREAT, n = 10; CTRL, n = 10).

Continuous blood pressure, electrocardiography, and impedance cardiography recordings were performed for 10 minutes 8 days before (BDC-8), three times during -6º head-down tilt (HDT) bed rest (i.e., HDT7, HDT31, HDT60), and twice after the cessation of bed rest (R+7 and R+13). During bed rest, data were collected in -6º HDT. To assess the effect of posture, data were recorded in in supine and sitting position before and after bed rest. All measurement sessions took place between 9 am and 1 pm.

Linear mixed models revealed during HDT a significant depression of vagal indices in both groups, independently from the treatment. After 60 days of bed rest, at R+7, HR in sitting position was significantly increased irrespective of the groups relative to BDC-8. Likewise, parasympathetic indices were significantly reduced in sitting position during the recovery in TREAT and CTRL. HR and HRV indices showed a trend towards recovery at R+13. In conclusion, these results showed that the nutritional cocktail, primarily targeted at counteracting bone and muscle atrophy was ineffective in mitigating cardiovascular deconditioning associated with prolonged bed rest.

The study was supported by the European Space Agency and by the German Aerospace Center (DLR, Deutsches Zentrum für Luft- und Raumfahrt) through grant 50WB1525.

THE ADVANTAGE OF SUPINE AND STANDING HEART RATE VARIABILITY ANALYSIS TO ASSESS TRAINING STATUS AND PERFORMANCE IN A WALKING ULTRAMARATHON

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Introduction. Extreme environments, like climatic exposition, arduous exercise, and sleep deprivation, pose great challenges for the human adaptive capacity and resilience. In this context, assessment of cardiac autonomic modulation in terms of Heart Rate Variability (HRV) may serve to monitor wellbeing and predict performance in extreme environments, such as ultramarathon (defined by course lengths >42.195 km) competition. Also, HRV assessment is commonly used to monitor training status. In athletes, HRV measurements are usually performed in the morning (after awakening) in the supine position. Whether a recording performed during active standing reveals additional information compared to a measurement obtained exclusively in the supine position remains unclear. We aimed to evaluate the association between short-duration HRV, assessed both in the supine and standing position, and (i) a low-intensity long-duration exercise (an ultramarathon performed exclusively by walking), as well as (ii) self-reported training experience.

Methods. Twenty-five competitors in a 100 km walking ultramarathon underwent pre-race supine (12 min) and standing (6 min) HR recordings at morning, whereas performance and subjective training experience were assessed at post-race. Subgroup assessment in relation to race performance differentiated between finishers (n = 14, who completed the 100 km racecourse) and non-finishers (n = 11, mean total distance 67 km). Regarding self-reported training status (i.e., mean km walked or run per week during race preparation), athletes were either assigned to highly (≥24.5 km/week) or poorly trained (<24.5 km/week). The significance level was set at $p < 0.05$.

Results. There were no significant differences in both supine and standing HRV assessed at pre-race between finishers and non-finishers. In finishers, a greater race velocity was significantly correlated with a higher decrease in parasympathetic

drive during position change [larger decrease in High Frequency power normalized units (HF_{nu}: r = −0.7, p = 0.01) and higher increase in the detrended fluctuation analysis alpha 1 index (DFA1: r = 0.6, p = 0.04)]. Regarding the association between pre-race HRV and training status, highly trained athletes accounted for higher HF_{nu} during standing compared to poorly trained competitors (+11.5, p = 0.01). Similarly, greater training volume (total km/week) would predict higher HF_{nu} during standing (r = 0.5, p = 0.01).

Discussion. Our results indicate that HRV assessment in both supine and standing position may provide additional information on the dynamic adaptability of cardiac autonomic modulation to physiologic challenges and therefore be more valuable for performance prediction than a measurement performed only during supine rest. Also, self-reported training experience may reliably relate to parasympathetic drive, therefore indirectly predicting long-term aerobic performance in ultramarathon walking races. Assessment of cardiac autonomic modulation in terms of HRV measurement may thus serve to predict the human physiologic response to, and performance during, different physiological challenges that may be assimilated as extreme environments.

OPTIC NERVE HEAD STADY IN SPACE FLIGHT

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Introduce. The eye status of cosmonauts in long-term space flight is studying in the International Space Station (ISS) actively. In a number of cases among cosmonauts were noted such signs of microgravity neuro-ophthalmic syndrome as flattening of the eye posterior pole, hyperopic refractive shift, chorioretinal folds and the optic nerve head (ONH) edema. The latter is one of the most serious symptoms of this syndrome. The refore its timely and objective diagnosis is important research.

Purpose. To estimate examination of the cosmonauts eyes in space flight for ONH edema diagnosis.

Methods. 10 Russian cosmonauts have made long space flight in the ISS over past 5 years and their eye status is analyzed in this study. The eye examination on the ISS board included fundus camera photo fixation and scanning the optic nerve head and peripapillary and paramaculary retina by Spectralis I and II optical coherence tomography (OCT). The ONH status is classificated by L. Frisen scale.

Results. Visual subjective examination of fundus photographs, multi-color images and OCT images were sated 4 eyes (20,0 %) with ONH edema II (3 eyes) and III stage according to L.Frisen scale. The chorioretinal fold and local decrease in the retinal nerve fiber layer (RNFL) below normal was got sight of one clinical observation, together with III stage ONH edema. The retina and ONH status was analyzed by generally accepted protocol of OCT examination: RNFL thickness and average retina thickness analysis. It was found that the size of the ONH edema was less than the diameter of the circle where the RNFL thickness is recorded. The reasons for the different distribution of RNFL thickness values over the peripapillary sectors, including the functional distribution of nerve fibers, localization of blood vessels, and the shape of the ONH have been determined. The cases defocusing of HRA images and circle dislocation of the RNFL thickness determine were analyzed, which led to changes in the OCT results. Possible errors that can occur during OCT survey in space flight are discussed.

Conclusion. The analysis of the RNFL thickness does not note of the presence or absence of small ONH edema at stages II–III on the L. Frisen scale which occurred in some cosmonauts on the ISS. Analysis of the average thickness of the peripapillary retina makes it possible to diagnose ONH edema without its classification according to the L. Frisen scale.

BIOREACTOR TECHNOLOGY AS KEY COMPONENT OF PROVIDING FOOD PRODUCTS ASTRONAUT IN FAR SPACE

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Any space flight into deep space connected with significant difficulties of providing food as astronauts making the flight and those arriving on the far planet. One of the ways to solve this problem is to use stem cells of animals and plants to build up cellular biomass when creating a food product in deep space. Generally known that stem cells can be stored in a frozen state for an unlimited time and after defrosting save their high proliferative and differentiation potential, these properties allow to be used them for to build-up cellular biomass in bioreactors. The aim of this work has been studying suitability pig stem cells for build-up cellular biomass in a bioreactor with aim to get a food product. The research had been performed with using pig stem cells isolated from red bone marrow, the basic nutrient medium was DMEM/F12 (cat. D8062-500ML, Merck Sigma-Aldrich,

Germany). In the the first stage, cells cultured in vials of different sizes from 75 cm2 to 175 cm2 (Corning, USA). Stem cells had been cultured on polystyrene microcarriers coated with pig collagen type 1 (cat. C-221-020 SoloHill Collagen, Pall, USA) in bioreactor CELLSPIN (INTEGRA Biosciences AG, Switzerland). As a result of cultivation for 8 days in a bioreactor had been received 50 ml of pig stem cell suspension concentrate that indicate their suitability further development of cell biomass scaling technology using microcarriers coated with collagen. However, the cultivation of cells in space connected with the influence of various cosmic factors, among which gravity is the key. Consequently, the question arises - Which is type of bioreactors acceptable for cultivation of stem cells in the conditions of gravity (weightlessness). Today, in the world is developing devices who allow us to study the impact of microgravity on living systems on Earth. The company Space Bio-Laboratories Co., Ltd. Japan developed a gravity controller «Gravity®» for simulate microgravity in which culture vials with cells are placed. However, it becomes obvious that it is necessary to move to search bioreactors and stem cell culture technologies who can provide industrial production of cellular biomass during the deep space flight taking into account the influence of space factors. Thus, only bioreactor technologies with using animal and plant stem cells can provide astronauts the necessary amount of biomass for food production, also astronauts can use thier personal stem cells that will allow creating individual biomedical cell products for the regeneration of astronaut's tissues in far space.

ASSESSMENT OF VISUAL FUNCTIONS DURING A 4-MONTH ISOLATION IN THE SIRIUS-19 PROJECT

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Introduction. Experiments on long-term isolation make it possible to partially simulate the conditions of space flights, and to assess the influence of artificial environmental factors on human performance. During the SIRIUS-19 project, the subjects were in isolation in a spaceship mock-up that simulates a spacecraft conditions. Such experiments make it possible to assess the effect of high visual load on the mechanisms of near vision, constant exposure to artificial lighting, and limited range of viewing distances. These factors can significantly affect a functioning of the visual system, that can be identified by changes in refraction, accommodation, sensitivity to flicker, visual acuity, contrast sensitivity, etc.

Purpose: to assess the stability of visual system functioning in conditions of long-term isolation in the spaceship mock-up.

Materials and methods. The study involved two groups of subjects: the «Crew» group, 6 healthy volunteers who were in isolation in the mock-up for 4 months (three men, average age 38.3 years, and three women, average age 30.6 years), and the control group leading a usual lifestyle, examined simultaneously with the «Crew» group (6 healthy volunteers, three men, average age 34.1, and three women, average age 34 years).

Monocular visual acuity for three distances (for near, for far, and for intermediate distance) was assessed using a computer program (developed at the IITP RAS, Russia). Refraction, accommodation microfluctuation coefficient, and accommodation response were assessed using an autorefkeratometer Righton Speedy-i k-model (Japan). The critical flicker frequency (CFF) was assessed using the «КЧСМ» device (Russia). Measurements were carried out in mornings and in evenings, every two weeks during isolation, once before and once after the isolation period (the survey schedule was the same for both groups).

Results. The visual function assessment results demonstrated the absence of significant changes in the measured parameters throughout the study, including comparison of the morning and evening data. When evaluating the accommodation data, some subjects from the «Crew» group showed a tendency to decrease (deterioration) of the accommodative response to the end of the isolation period. However, these data require verification, both due to the small sample size and the possibility of the influence of habituation to the procedure or unclear instruction before measurement. There was also a statistically significant increase in CFF in the «Crew» group (Wilcoxon test, $z = -2.357$, $p = 0.018$). In the control group, no increase in CFF was found. It is worth to note that the observed changes in CFF were not clinically important, but this trend also requires further verification.

Conclusions. During the 4-month isolation in the spaceship mock-up, the assessed visual functions of the «Crew» group remained stable, and no clinically significant changes were found. We can conclude that 4-month isolation does not affect visual performance. However, the revealed tendencies towards a decrease in the accommodative response and an increase in CFF to the end of the isolation period indicate the need for a more thorough study.

DYNAMICS OF VISUAL ACUTE AND CONTRAST SENSITIVITY IN WINTER CONDITIONS AT THE «VOSTOK» ANTARCTIC STATION

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Introduction. Adaptation of the mechanisms contributing to the visual system functioning under the stressful environmental conditions is a cutting-edge issue in space medicine. It is especially important in view of long-term space travels.

We describe a study of visual acuity and contrast sensitivity that was carried out to expand understanding of visual system stability in Antarctic winter stay conditions.

Purpose: To obtain new data on the visual system's functional activity during the prolonged human stay in extreme Arctic environmental conditions at the «Vostok» station.

Material and Methods. Visual acuity and contrast sensitivity data were assessed in nine healthy volunteers aged 33 to 65 years. The measurements were conducted once before an 7 times during the nine-month winter stay at the «Vostok» Antarctic station.

All measurements were conducted with optical correction (if needed). Visual acuity was assessed binocularly at the distance of 1 m by means of interactive computer program «Tiptop» developed at the IITP (Russia); screen luminance was 160 cd/m^2.

Contrast sensitivity function was studied monocularly using the computer program «Visocontrastometry» (Russia) at the distance of 1.5 m in the range of spatial frequencies from 0.4 to 30 cycles/deg.

Results: The visual acuity and contrast sensitivity data, obtained in the mornings and evenings, were stable during the whole study. Average visual acuity of the group before the winter stay was normal (1.0 dec.units, SD = 0.25); the variations during the stay were from 0.93 to 1.02, but no statistically significant differences were found.

The data of contrast sensitivity function at the end of winter stay were higher than the background ones, mainly in the range of low (0.4–1.8 cycles/deg) and high (21–24 cycles/deg) spatial frequencies ($P < 0.05$).

Discussion: During 9 months of observation, no significant changes in visual acuity data were found. This indicates the relative stability of visual acuity as an integral indicator of the functionality of visual system at high contrast under extreme environmental conditions during Antarctic winter stay. Contrast sensitivity data showed a higher sensitivity to stressful conditions. An increase in contrast sensitivity in the range of low and high spatial frequencies at the end of the winter stay may indicate the contribution of compensatory adaptation mechanisms of the visual system under prolonged exposure to the stressful environmental factors.

Conclusion: The nine-month observation during the Antarctic winter stay did not reveal significant changes in visual acuity of healthy volunteers. Changes in contrast sensitivity may indicate higher sensitivity of the corresponding mechanisms to the prolonged exposure to the stressful environmental factors and the contribution of adaptation mechanisms.

GENDER CHARACTERISTICS OF THE METABOLIC REACTIONS OF VOLUNTEERS IN AN EXPERIMENT WITH 120-DAY ISOLATION IN A PRESSURIZED VOLUME AGAINST THE BACKGROUND OF STRESSFUL INFLUENCES

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Introduction. Studies on the International Space Station have found that gender-mixed crews perform their functions more effectively than purely male ones [Vakoch D.A., 2011]. However, the reactions of male and female bodies to the effects of space flight (SF) factors are different due to gender-related variability and the direction of metabolic processes. The current level of medical technology does not allow for a comprehensive examination of cosmonauts in flight. The model with isolation in a hermetic volume (IHV) reproduces the effect of the main SF factors on the body, with the exception of microgravity, and allows us to simulate its main stages [Stuster J., 2005].

The purpose of the research. To study the gender characteristics of the metabolic reactions of volunteers (VL) in an experiment with a 120-day IHV against the background of stressful influences.

Materials and methods. In the experiment with a 120-day IHV SIRIUS 18/19, simulating a flight to the Moon with a landing on its surface, 6 volunteers aged from 27 to 46 years participated: 3 men and 3 women. In the course of the IHV, they were periodically influenced by stress factors: intense physical activity (IFA), imitation of intense extravehicular and on-planetary work, operator activity in conditions of lack of time, and sleep deprivation. The values of 47 biochemical parameters reflecting the state of internal organs and tissues, as well as the main links of metabolism, were studied in the VL blood serum.

Results and discussion. The influence of a complex of stress factors in the dynamics of IHV with the leading role of IFA was realized in a pronounced activation of skeletal muscle activity, a decrease in the filtration capacity of the kidneys, and a strain on liver functions. The activation of energy-synthetic processes in mitochondria was observed, provided by the substrates formed as a result of the activation of lipolysis processes. There were signs of increased protein catabolism and an increase in blood products of nitrogen metabolism. Gender-specific features of metabolism were characterized by a greater severity of the above-mentioned processes and activation of adjacent metabolic links in men. In addition to shifts in energy metabolism, they showed signs of acid-base imbalance and significant changes in pigment metabolism.

Conclusion. The metabolic reactions of VL in the experiment with 120-day IHV were determined by the action of a complex of stress factors, primarily IFA. They were characterized by an increase in the activity of muscle enzymes, activation of energy synthesis reactions in mitochondria, activation of lipolysis, changes in protein and nitrogen metabolism, tension in liver function, and a slowdown in the glomerular filtration rate of the kidneys. Gender-specific features of metabolism were characterized by a greater severity of metabolic changes in men. Given the absence of clinically significant changes in the values of the studied parameters, the detected shifts can be interpreted as adaptive.

«PLASMA – BIOLOGICAL OBJECT» INTERACTION: STUDY OF BASIC MECHANISMS

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The aim of the work was to compare the effect of different exposures of cold plasma on the state of free-radical processes in the biological fliud.

Material and methods. In vitro experiment was performed on 15 blood samples of healthy volunteers (3.5 ml each). Each sample was divided into 7 equal portions, the first of which was a control one (no manipulations were performed in it), the rest were treated with cold helium plasma. The duration of exposure for the experimental portions (second-seventh) was 1, 2, 3, 5, 10 and 15 minutes, respectively. The distance from the end of the «plasma torch» to the surface of the biological fluid was equal to 1.0-1.5 cm. The duration of exposure after cold plasma treatment is 5 minutes. Cold plasma was produced using a special device using the principle of microwave-induced ionization of the gas stream and developed at the Institute of Applied Physics of the Russian Academy of Sciences (Nizhny Novgorod). As a plasma carrier gas, we used balloon helium of grade A (purity level - 99.99%). The intensity of free radical processes in blood plasma was studied on the apparatus BHL-06 (Nizhny Novgorod, Russia) by Fe-induced biochemiluminescence. The level of malonic dialdehyde (MDA) in red blood cells was assessed using a test kit (JSC «AGAT», Russia). The results were processed using the Statistica 6.0 program.

Results. The conducted studies allowed us to establish that the level of maximum photo-flash of biochemiluminescence in blood samples progressively increases with increasing duration of treatment with cold helium plasma. At the same time, it is important to emphasize that at low exposures (1–2 min.), the studied parameter shows a tendency to increase (+11.0 and +14.1 % relative to the control sample, respectively; $p < 0.1$ only for the second mode). A rapid increase in the level of maximum flash light is observed only starting from 3-minute processing of the biological medium (+49.7 %; $p < 0.05$) and reaching a maximum exposure of 15 min. (an increase of 2.27 times compared to the intact sample; $p < 0.01$). The presence of such an unusual effect of cold plasma is also evidenced by the dynamics of the overall antioxidant activity of the biological medium. It was found that short-term (1–2 min.) treatment of blood samples with helium cold plasma contributes to an almost identical increase in the value of the indicator (by 18.0 and 20.6 % relative to the control; $p < 0.05$ for both cases), while 3-minute exposure demonstrates the level of the parameter that does not differ from the intact sample. This confirms the results of our previous in vivo studies [4]. Longer exposures of the studied factor (5 minutes or longer) reduce the antioxidant reserve of biological fluid (by 21.9–34.2 %; $p < 0.05$). The results of chemiluminescent studies are fully confirmed based on the analysis of the dynamics of the standard indicator of the intensity of free radical processes-the concentration of malonic dialdehyde in blood plasma. It was found that its level increases insignificantly with short exposure to cold plasma (1- and 2-minute treatment), increasing only by 5.2 and 9.7 % compared to the control sample ($p > 0.05$). On the contrary, starting from the 3-minute mode (+36.0 %; $p < 0.05$), an almost linear increase in the parameter value was recorded, up to the maximum exposure (15 min.), at which there was an increase in the concentration of the studied secondary product of peroxidation by 2.50 times ($p < 0.05$).

Conclusion. Our research allowed us to establish that the nature of the response of antioxidant systems of the blood to treatment with a stream of cold helium plasma is directly determined by exposure, as evidenced by the results of chemiluminescence assessment of the intensity of free radical processes and total antioxidant activity, as well as the dynamics of the concentration of malonic dialdehyde. At the same time, the short-term processing mode of biological fluid allows us to establish the presence of a two-phase influence of the factor on oxidative processes («phenomenon of the antioxidant window», the limit of which for our exposure conditions was an exposure of 2 min.).

CRYSTALLOSCOPIC TEST-SYSTEM FOR COLD PLASMA EFFECTS DETECTION

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Plasma medicine is a dynamically developing field that is located at the intersection of biology, medicine, physics and chemistry and integrates their achievements. Given the specifics of the functioning of biological objects, the main subject of plasma medicine is the so-called «cold plasma», which has, in contrast to the initially generated, a temperature in the range of 20–50°C. This prevents thermal damage to cells and / or tissues. It should be noted that in this direction, the physical basis of generation and characteristics of cold plasma have been significantly more studied, while the biological effects of this factor have not been fully studied. Thus, the features of activation of free-radical processes that serve as the basis for the antibacterial action of cold plasma are shown. However, such a response of biological systems associated with the intensive generation of reactive oxygen species in them under the considered influence is manifested only in conditions of long-term exposure. The effect of short-term exposure to cold plasma on biological objects is significantly less detailed, but the available data on significantly lower intensity of radical formation in this mode suggest a different nature of the effect of this type of exposure.

The aim of this work was to evaluate the modulating effect of helium cold plasma on the crystallogenic and dielectric properties of blood plasma.

Material and methods. Blood samples from 25 healthy volunteers were used. Each blood sample was divided into 2 equal portions (2 ml in each portion). The first portion was intact, and the second one was treated with a stream of cold helium plasma for 60 seconds. The helium plasma was generated by a special device using the principle of microwave gas ionization. To conduct a crystalloscopic study, all samples of biological fluid were centrifuged according to the standard method until plasma was obtained. Then we studied the intrinsic crystallogenic activity of blood plasma by classical crystalloscopy. The description of dehydrated blood plasma samples was performed morphologically and using a system of visuametric parameters that characterize the qualitative and quantitative aspects of the process of crystallization of the biological medium (crystallizability, index of structure, facia destruction degree, the clearity of its marginal zone).

Results. Our experiments allowed us to establish that the influence of the considered factor, without having a thermal effect, contributes to the transformation of the physical and chemical properties of the biological medium. In particular, the modulation of the dielectric properties of whole blood is manifested in a decrease in the permittivity of the biological fluid. This, in turn, may be due to the redistribution of compartments of free and bound water in it. The second effect of cold plasma revealed in the study is a change in the crystallogenic activity of blood plasma. It was found that the studied factor provides an increase in the crystallogenic potential of the biological medium, and these shifts can be interpreted as positive, since an increase in the density of crystal elements in the micro-preparation is accompanied by a significant decrease in the degree of facies destruction. At the same time, the oxidative potential of the ionized gas stream potentially contributes to the increase in the phenomena of oxidative modification of blood plasma proteins, which is realized as a narrowing of the edge belt of the crystalloscopic facies. On the other hand, such changes in the aggregate do not indicate the presence of destructive effects of cold helium plasma on human blood during short-term (for 60 s) exposure.

Conclusion. We establish that short-term (for 1 min) treatment of human blood with helium cold plasma has a pronounced modulating effect on the integral parameters of the biological medium that characterize its physical and chemical properties. It is shown that this factor increases the crystallogenic potential of the biological medium. This is manifested in an increase in the density of crystal elements without significant complication and a decrease in facia destruction degree.

BIOMEDICAL TRAINING OF THE FIRST MANNED SPACE FLIGHT

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The first manned space flights of the Soviet Union largely took place thanks to the Scientific Research and Test Institute of Aviation Medicine. In the Institute there were formed the foundations of biomedical training of manned space flights. In the interests of spaceflight were developing air regeneration, water supply, support of temperature, pressure and gas control systems, as well as means of rescue and survival. November 3, 1957 all this allowed to implement the orbit flight of the dog Layka. By Regulations of the Soviet Government of January 5, 1959 «On the medical selection of candidates for cosmonauts» and on May 22, 1959 «On the preparation of a human for space flights» the Institute was engaged in the formation of a detachment of cosmonauts and their preparation for the first space flights. The Central Aviation Hospital

took part in the selection of the cosmonauts. By the Air Force Main Headquarters Directive of January 11, 1960, a unit of candidates for cosmonauts was created at the Institute. On May 7, 1960, the Air Force Commander-in-Chief approved the Regulation on the Cosmonaut Training Center in operational subordination to the Aviation and Space Medicine Service. The Institute's staff were engaged in training and medical providing of Yuri Gagarin's space flight. For biomedical training of this flight, the Institute was awarded the Order of the Red Star, and its 92 employees were been awarded orders and medals. In the future, the Institute took part in the preparation of flights by G.S. Titov, A.G. Nikolaev, P.R. Popovich, V.F. Bykovsky and V.V. Tereshkova. By Regulations of the Soviet Government on October 28, 1963 there were established the Institute of Space Biology and Medicine, which in 1965 became the Institute of Biomedical Problems of the Ministry of Health. Its staff formed largely from the personnel of the State Research Institute of Aviation and Space Medicine. Subsequently, these organizations worked closely together to conduct space research on the Voskhod, Soyuz, Salute, Mir, Buran and International Space Station programs. There were been developed a system to prevent the adverse effects of weightlessness on the body of crews of orbital stations. They were determined the sanitary and hygienic parameters of the environment and the conditions of activity in order to improve the performance and providing the safety of the cosmonauts. They created methods and means to improve performance in flight, selected modes of work and rest of cosmonauts, developed methods of prevention of fatigue and active rest in flight. A significant result was the creation of a system of psychophysiological characteristics of human accounting during the development and using of space technology. Today, the safety of spaceflight also depends on taking into account the psychophysiological capabilities of human in the creation of space technology and in spaceflight. To do this, it is necessary to develop an experimental base and methodology to train personnel and to create conditions for exchange of views on the current problems of ensuring the psychophysiological reliability of cosmonauts.

DAY OF TRIUMPH OF COSMONAUTICS

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The preparation of Yuri Gagarin's first manned space flight was attended by the staff of the State Scientific-Research and Test Institute of Aviation and Space Medicine. On April 8, 1961, a solemn meeting of the State Commission was held under the chairmanship of K.N. Rudnev. V.I. Yazdovsky and A.D. Seryapin were present at the meeting from the Institute. S.P. Korolev said that the ship is ready, all equipment and equipment are checked and working. At the suggestion of the Air Force Command the Commission approved the first cosmonaut Yuri Gagarin, and the reserve German Titov. On the evening of April 11, a pre-flight medical examination of the cosmonauts was carried out by L.G. Golovkin, F.D. Gorbov, A.R. Kotovskaya, I.T. Akulinichev, A.D. Serapin and A.V. Nikitin. They checked the health of the equipment, pasted sensors, conducted a medical survey and examination, measured blood pressure, pulse and prepared a conclusion about its functional readiness. They were led by V.I. Yazdovsky. At 5:30 a.m. on April 12, 1961, E.A. Karpov woke up Yuri Gagarin and Herman Titov. At 8 a.m., an hour before the arrival of the cosmonauts, O.G. Ivanovsky and N.P. Kamanin took the elevator to the spacecraft and checked the cipher of the logical lock needed to switch to manual control. I.T. Akulinichev checked the overlay of sensors, and V.I. Svershchek and F.A. Vostokov helped the cosmonauts to wear a spacesuit. On the bus cosmonauts were taken to the launch pad. The report was made to the chairman of the State Commission. Then, accompanied by E.A. Frolov, Yuri Gagarin went up to the stairs, and they went up to the lift. At the elevator, at the lift and at the hatch of the spaceship Yuri Gagarin was accompanied by L.G. Golovkin, O.G. Ivanovsky, F.A. Vostokov and camera operator V.A. Suvorov. On the elevator Yuri Gagarin climbed to the upper platform of the launch vehicle maintenance farm to the Vostok ship. One of those who helped Yuri Gagarin to stay in the catapult chair and reported on the readiness of the protective equipment of the cosmonaut for space flight was L.G. Golovkin. He was engaged in medical-technical and physiological problems of designing spacesuits and ensuring the safety of astronauts in emergency and extreme space flight situations. These studies were carried out by the staff of the laboratory of the Institute, established in 1956 at the plant «Star». In 1960, a medical department was established at the «Star» plant, headed by A.G. Kuznetsov. The triumph of domestic cosmonautics on April 12, 1961 was largely provided by the specialists of various organizations to study the effects of space flight factors on the human body and develop life support systems and means of rescue in extreme situations. A special role in the success was played by the presence of a scientific foundation in the study of the effects of various factors on the human body and in the development of methods, means and ways to ensure the safety of professional activities.

ROLE OF STRESS IMPACTS OF WEAKENED GEOMAGNETIC FIELD ON DROSOPHILA MEMORY FORMATION

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Introduction. Long-term space flights inevitably raise the issue of accounting for all factors of external influence on cosmonauts. Among such factors, the impact of weakened geomagnetic field (WGF) has received unreasonably little attention even though the Earth's static magnetic field possesses a unique feature – it has an enormous ability to penetrate into all biological systems. In their work M.E. Lobashov and V.B. Savvateev (*Physiology of daily animal rhythm*. 1959) obtained unique results about expanding the organism's abilities to adapt by training higher nervous activity characteristics through the formation of alimentary conditioned reflexes in response to stimuli which exhaust the nervous system. The formation of a conditioned response facilitated the ability to overcome stress impact, adapt to restrictive conditions and change nervous system operations. Drosophila is an adequate model for such investigations because sequence analysis of its genome shows that it is 60 % homologous to the human genome and approximately 75 % of genes responsible for human diseases have homologues in Drosophila.

The aim of the work was to verify the hypothesis about the existence of common mechanisms between stress reactions and cognitive functions.

Materials and methods. All experiments were performed in Koltushi (Leningrad Region) during the study of Drosophila memory formation in the paradigm of conditioned-reflex courtship suppression. Static geomagnetic field in Koltushi (B = 50μT) was weakened by K = 35 using the shielding cylindrical camera covered with AMAG-172 screening material. All measurements of magnetic field induction B were done by magnetometer HB0302.1A (0.1 μT – 100 μT, resolution 0.1 μT, Russia).

Results. Complex analysis of WGF impact on Drosophila genome's transcriptional activity and on Drosophila learning ability along with medium-term memory formation detected impairment of medium-term memory in wild type Canton-S strain. By contrast, in agn^{ts3} mutant (locus agnostic with the gene for LIMK1 – key actin remodeling regulator) this stress impact results in the recovery of learning ability and memory formation. Moreover, we observed the dependence of transcriptional activity on LIMK1 gene structure. Apparently, WGF targets actin remodeling cascade, which determines the functioning of transcriptional factors, axons and dendrites that ensure nervous system flexibility. At the same time, WGF impact on cells primarily affects the condition of mitochondria and superoxide dismutase operations and causes a disruption in superoxide radicals' dismutase reaction and accumulation of active oxygen forms in cells with aerobic respiration. It is free radicals that serve as modulators of actin cytoskeleton and actin-associated proteins.

Conclusion. WGF influence on Drosophila memory formation exhibits the similarity of stress impact mechanism and the formation of plastic changes in the nervous system.

COORDINATION AMONG THE LOWER LIMB MUSCLES DURING LOCOMOTION ON THE PASSIVE-MODE TREADMILL IN MARS500 AND IN THE LONG-TERM SPACE FLIGHT

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Introduction. Force-sharing between synergists and their coordination with antagonists appears as important paradigm for motor control and rehabilitation. In Mars500 project, we reported a speed-dependent time gap between recruitment of the lower limb synergists during locomotion on the leg-driven treadmill (Meigal, Fomina, 2016). Here, we aimed at comparing coordination among the lower limb muscles under the condition of space flight (SF) with the data from Mars500 project.

Methods. Surface electromyogram (sEMG) was obtained with «Miograf» device (Biofizpribor, Russia) in SF, and «Neiro-MVP-8» (Neirosoft Ltd., Ivanovo, Russia) in Mars500 (Meigal, Fomina, 2016) from vastus lat. (VL), tibialis ant. (TA), gastrocnemius lat. (G), and soleus (Sol) muscles, at 3 study points - before (preSF), during (inSF) and 2 weeks after a long-term SF (postSF) during walking/running on the passive-mode (leg-driven) treadmill (BD-2, IMBP, Moscow, Russia) in MO-3 test, at 4 different speeds (4-11 km/h, altogether 11 min), on board of the International Space Station (ISS). During MO-3 test, the subjects were axially loaded at 50-70% of their individual earthly body weight with a special training-loading suit. Bursts of sEMG of each step were identified, stored and further characterized with mean frequency (MNF, Hz) and average amplitude

(AEMG, mV). Inter-muscle coordination of Sol and G was evaluated on sEMG with the time gap between moments of their recruitment in all step cycles (ΔSol/G, ms), as in Mars500.

Results. 1. In ISS experiment, dynamics of sEMG characteristics: a) at all study points, the AEMG in VL, G and Sol has systematically increased with increase of the locomotion speed; b) in TA, AEMG has decreased, with growth of the locomotion speed, at inSF point; c) in Sol AEMG was increased at all locomotion speeds in the inSF condition in comparison to preSF and postSF; d) MNF did not regularly change across the study. In Mars500, AEMG was growing along with speed growth in all muscles. 2. Dynamics of ΔSol/G: a) in the preSF condition, at the lowest speed of locomotion (4–6 km/h), Sol was recruited 100 to 500 ms earlier than G, but with growing speed ΔSol/G has diminished to 0 ms, what generally matches the result of the ground-based Mars500 experiment; b) within SF, at 4-6 km/h, ΔSol/G was 100 to 0 ms, and it has reversed to -200 ms at 11 km/h, what means that G started recruiting prior to Sol. Such reversed order was persisted also at 4-6 km/h speed at the end of the test. c) PostSF, ΔSol/G was around -200 ms at 4–6 km/h, 0 ms at higher speeds, and again -200 ms at 4-6 km/h at the end of the test.

Discussion. 1. Increased sEMG amplitude of Sol during locomotion at SF suggests its specific role in adaptation to SF. 2. Coordination between two synergists (Sol and G) was modified during and after SF across all speeds of MO-3 test in the direction of earlier recruitment of G. In sum, this suggests profound fatigue of Sol in SF compensated with its increased activity and delayed recruitment. So far, that assumption is not supported by the MNF dynamics.

Conclusions. Locomotion on the passive-mode (leg-driven) treadmill can be regarded as a highly efficient countermeasure for the negative effects of SF. Additionally, it can be considered as a promising research tool to study muscle coordination.

MITIGATING MUSCLE AND BONE LOSS DURING SPACEFLIGHT: GSK3 AS A POTENTIAL CELLULAR TARGET

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Spaceflight is a physiologically demanding task. It is well established that prolonged exposure to microgravity leads to rapid decrements in exercise tolerance, muscle mass, and bone mineralization. In muscle, spaceflight causes muscle atrophy and a fiber type shift from slow-oxidative to fast-glycolytic, which altogether compromises muscle strength and fatigue resistance. In addition, because of the lowered loading stimuli with spaceflight, there is a reduction in bone mass caused by an imbalance between bone resorption and bone formation. Countermeasures that prevent bone and muscle loss will not only enable long-term space missions, but could also inform us here on earth as global population aging will undoubtedly raise the rates of osteoporosis and sarcopenia. Glycogen synthase kinase 3 (GSK3) is an enzyme found in muscle and bone, expressed in two isoforms – GSK3α and GSK3β. In muscle, GSK3 negatively regulates muscle mass and the oxidative myogenic program, by inhibiting Wnt/β-catenin signalling and counteracting the calcineurin-NFAT axis. Recent work from our lab and others has shown that inhibiting GSK3 can promote myoblast fusion, fatigue resistance, and the oxidative phenotype in non-transformative models as well as ground-based analogs of spaceflight. In bone, GSK3 is a well-known inhibitor of the anabolic pathway activated by Wnt/β-catenin signalling; and we and others have shown that GSK3 inhibition can enhance osteogenesis. Taken together, inhibiting GSK3 may provide a viable strategy towards minimizing the bone and muscle loss and remodelling that occurs with spaceflight. Indeed, exercise is the primary countermeasure used to combat spaceflight induced muscle atrophy and bone degradation. It is possible that some of these effects are, at least in part, mediated by GSK3 inhibition. This introduces the possibility that inhibiting GSK3 in addition to regular exercise may provide a synergistic effect that further attenuates muscle and bone loss.

MSG – MOVEMENT SPACE AND GROUP HEALTH IN A RESTRICTED AREA

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MSG (Movement Space and Group health) is an exploratory study to examine the relationship between sociological-psychological functioning and effective physical space for the analog astronaut at the station. The journey to Mars and living there involve extreme and unique capsule-like conditions. Previous studies of analogous Mars missions showed that it is difficult to generalize from Earth-bound capsule environments, because these do not suffer the mental strain of delayed communication and prolonged monotony as much as long duration spaceflight. The team reported that the most difficult moments were delayed communication and monotony, especially in the second half of the journey.

In the design of the living unit, first and foremost, considerations of survivability and functionality are taken, and these dictate a limited area. The spatial constraints, especially in the confinement of a spacecraft or a Mars base, will have a significant impact on crew social dynamics. The patterns of movement in the confined space of the habitat therefore become

a factor that maximizes their usefulness and may be of significance to the personal and group well-being of the task team. In this study, we aim to describe the way the crew utilizes the habitat and how the habitat's limited space might affect the crew psychological well-being.

Our main research objectives are:

1. Identify individual and group movement patterns of the team throughout the mission
2. Correlate individual and group movement with individual and group well-being.
3. Analyze the correlation between individual and group well-being movement patterns in the different task descriptors (task-group, non-task-group and private).
4. Establish a reliable and easily implemented measure of individual and group psychological functioning on the timeline and in general.

Rationale for the Project. By measuring movement inside the habitat, we strive to better understand how the spatial design facilitates or interfere with group behaviour and functioning. Doing so, we can provide insight that will lead to design guidelines that will ensure more resilience and robust crew performance. We seek for measures that could be implemented in other types of missions and would be relatively easy to implement. It will also allow for the development of indicators for identifying unwanted traffic patterns by looking at the different task descriptors. The experiment will contribute to understanding factors relevant for physical, social, and mental crew health.

THE EFFECTS OF 120 DAYS CONFINEMENT DURING THE SIRIUS PROJECT ON PHYSIOLOGICAL KINETICS AND INHIBITORY CONTROL

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Purpose. Sojourns in microgravity, like on the international space station (ISS) and especially during future long-term space travel, affect cardiorespiratory and cognitive parameters with influences on mission success, fitness, and overall well-being. Countermeasures are investigated with respect to their feasibility in space, time-efficiency, and overall beneficial effects on physical and cognitive performance. While both interval (INT) and continuous (CON) physical exercise training show positive effects on heart rate (HR) and oxygen uptake (VO2) capacities and kinetics in terrestrial settings, research for space application is still pending. Furthermore, in laboratory conditions, physical exercise positively interacts with cognitive performance, whereas confinement is known for the detrimental effects of inactivity and less external stimuli.

Therefore, this interaction should be implemented in the analysis of countermeasures for confinement and microgravity-contexts. We expected (I) negative effects of confinement on cognitive performance and (II) physical fitness improvements, especially from INT.

Methods. Six participants (34 ± 6 years, 3 females) spent 120 days in confinement, conducting eight weeks of CON, followed by eight weeks of INT aerobic treadmill exercise in a crossover design. Changes in cardiorespiratory fitness and cognitive performance were assessed with an exercise test protocol, including pseudo-random work rate changes (PRBS), constant workrate phases, and incremental exercise before the start of confinement (PRE), five times during confinement (mission day (MD) 9 (±1;), 29 (±1), 57 (±1), 87 (±1), and 117 (±1)), and after the termination of the mission phase (POST). HR was measured beat-to-beat, and VO2 assessed breath-by-breath. From interpolated 1 s data, kinetics information were derived using time series analysis on the PRBS part. Capacities of VO2 and HR were determined from the last 30 s of incremental exercise. Within the exercise test, the Eriksen Flanker task tested inhibitory control during REST, constant workrate at 3 (LOW), 6 (MID), and 9 km h-1 (HIGH), and during recovery (REC).

Results. For peak values significant time effects for HR ($P = 0.025$), VO2 ($P = 0.012$), and respiratory exchange ratio (RER) ($P = 0.001$) with lower values during confinement were shown. Kinetics of HR and VO2 revealed a significant time effect (both < 0.05). CON and INT exercise both seemed to speed HR kinetics during the mission with slightly better effects for INT. Inhibitory control was neither altered during rest, constant work rate nor at recovery by 15 weeks of confinement.

Conclusion. While the positive effects of INT and CON aerobic exercise, as known from laboratory studies, were also evident in HR kinetics during confinement, no improvement can be reported for VO2 kinetics. This might be due to the lack of general physical activity during confinement, which was merely compensated and not improved by the applied exercise countermeasure. In addition, this study proved the successful implementation of cognitive testing within our physical exercise test during confinement. Reaction times (RT) and accuracy (ACC) of the Eriksen Flanker task were not significantly altered.

Yet, descriptively slower RTs were observed during confinement compared to PRE and POST and might be attributed to less external stimuli, a decline in participants' mood, or general confinement effects.

SEX-BASED DIFFERENCES IN MUSCLE RESPONSE IN RATS EXPOSED TO MICRO- AND PARTIAL- GRAVITY ANALOGS

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For decades, scientists have used ground-based analog models to mimic weightlessness and assess muscle deconditioning. Recently, a new model of quadrupedal unloading was validated in rats to mimic partial gravity environments. However, despite its widespread use, few studies have aimed at comparing the muscular response to unloading in males and females concomitantly. Since biological sex plays a critical role in muscle physiology and that reproductive hormones participate in muscle homeostasis, we aimed to assess the sex-based differences in response to two different unloading protocols. Henceforth, using both hindlimb suspension (HLS) and partial weight-bearing at 40% of normal loading (PWB40) to mimic Mars gravity, and normal loading (NL), we assessed the declines in muscle force, function and size during a 14-day experiment in adult rats.

Adult outbred Wistar rats (14 wk-old) were assigned to each group for 14 days, and longitudinal assessments included body weight, food intake, limb girth, grip force, and force production during titanic nerve stimulation. At the end of the study, the triceps surae was harvested, weighed, and histomorphometry was performed to determine cross-sectional area (CSA) and fiber type. All protocols were approved by the institutional IACUC.

During HLS, males and females had similar variations in body weight and limb girth. However, females' grip force was significantly less impaired by unloading, with a 22.4 % decline at day 14 compared to a 53.2 % decline in males (effect of time x sex x loading $p = 0.0026$). Similarly, force production was decreased in males during both plantar and dorsi flexion, while females remain stable throughout the study. Ex vivo analyses revealed a similar atrophy of the gastrocnemius muscle in males and females, however females exposed to HLS displayed a significantly smaller atrophy in the soleus muscle ($p < 0.05$).

During PWB40, male animals experienced significant declines in body weight, limb girth and grip force while females did not. Similarly, gastrocnemius mass was significantly lower in PWB40 males compared to the controls while it was not impacted in females despite a small reduction in myofibers CSA.

Finally, in the soleus, a significant atrophy was observed in males exclusively. Taken together, our results highlight the strong sex-based differences in adult rats exposed to varied degrees of mechanical unloading. Indeed, females appear to preserve muscle function and size in comparison to their male counterparts. These studies using both sexes concomitantly are very rare in the literature, and our results present a compelling case for addressing these differences in the future when assessing muscle disuse, but also when investigating the potential benefits of new countermeasures.

This work was supported by NASA (NNX16AL36G and 80NSSC19K1598.

THREE DAYS OF DRY IMMERSION REDUCE MITOCHONDRIAL RESPIRATION RATE IN M. SOLEUS IN WOMEN

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Long-term inactivity has a negative influence on the functional characteristics of skeletal muscles, including mitochondrial density, oxidative capacity, and aerobic performance. However, it is still unknown how quickly these changes occur. The aim of this study was to evaluate the effect of 3-day dry immersion on the mitochondrial respiration rate in m. soleus (major postural skeletal muscle) in women.

Six women of reproductive age (25–40 years old) were exposed to dry immersion for 3 days. Before and after dry immersion, tissue samples were taken from m. soleus. Maximal mitochondrial respiration rate was measured in permeabilized muscle fibers using an Oxyghraph polarograph by consistent addition of malate + pyruvate + glutamate (ADP independent respiration rate (phosphorylation) of complexes I + III + IV + V), ADP and succinate (ADP stimulated respiration of complexes I + III + IV + V and (I + II) + III + IV + V respectively). The maximum oxidation rate (respiration of complexes (I + II) + III + IV) was estimated by adding the FCCP uncoupler (Carbonylcyanide-4- (trifluoromethoxy) phenylhydrazone).

Exposure to dry immersion led to a decrease ($P < 0.05$) in the rate of ADP-independent respiration by 10–15 % and ADP-stimulated respiration by 25–30 %, as well as to a decrease in the maximum oxidation rate by 25–30 %.

Thus, it has been shown that even three days of dry immersion exposure markedly reduce the mitochondrial functions in m. soleus. This rapid reduction could apparently be associated with initially high oxidative capacity and high content of type I fibers in this muscle. A decrease in the functions of mitochondria can be caused by both changes in the respiration regulation and a decrease in the content of mitochondrial enzymes.

BIOSENSORY MEDICAL TECHNOLOGY FOR NON-INVASIVE DIAGNOSTICS OF OXIDATIVE STRESS BASED ON THE BIOMARKERS IN EXHALED BREATH

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Human exploration of deep space will require the development of medical technologies capable of providing early and non-invasive diagnostics of human health in flight. One of the promising steps in this direction is the creation of medical technology based on the low molecular weight volatile metabolites - biomarkers of lipid peroxidation in the exhaled breath of a person during physiological adaptation to space flight conditions with the determination of the human reversibility limits and health risk assessment.

Volatile organic compounds (VOCs) - biomarkers of oxidative stress in the exhaled air of 20 healthy volunteers have been analyzed by chromatomass spectrometry, in two series of studies, including 1- and 2-hour breathing of 100 % oxygen, at normal pressure, in a sitting position. The concentrations of VOCs in exhaled air were sampled using the Gerstel (Germany) sorption tubes - 2 tubes for each sampling point: one tube with Tenax TA sorbent and one tube with Tenax / Carboxene sorbent. The sampling of the alveolar part of exhaled air was controlled by CO2 concentration using ReCIVA breathing mask analyzers (Owlstone, Great Britain).

From about 50 VOC's detected in the breath samples, the major biomarkers identified by GC-MS are: 1) 3-methylhexane, 2) 2-methylhexane, 3) heptanone-2, 4) isoprene, 5) 3-methylbutanal, 6) heptane, 7) 2-methylpentane.

The theoretical assumption that several biomarkers being combined could provide a more reliable determination of the LPO activity, although each of them, taken individually, is insufficient for the diagnosis, showed the need to use an alternative method for the evaluation of results. The discriminant analysis allows to simultaneously take into account the change in the dynamics of all 7 biomarkers, reduce the dimension of the initial data, visualize changes in the dynamics of biomarkers for further interpretation, leave the most informative biomarkers in the model and remove from the model markers that have an insignificant effect on the forecasting model. Data discrimination was carried out using Statistica Statsoft ver.8. The stepwise mode which is based on minimization of the Wilkes coefficient (λ) after the inclusion of each new biomarker-predictor in the regression equation has been applied. The analysis was automatically stopped at the 5th step. Thus, the Statistica Statsoft algorithm included 5 biomarkers into the model (3-methylbutanal, heptanone-2, isoprene, 3-methylhexane, 2-methylpentane). Two biomarkers (2-methylhexane and heptane) were excluded from the analysis due to their low information content. The developed model was tested by the cross-validation method. It is shown that the forecast accuracy of the preliminary mathematical model is 70 %. The equipment is currently being qualified for use on board the ISS.

SLEEP LOSS AND HIGH TASK DEMAND LEAD TO FAST AND SLOPPY DECISION-MAKING: EYE-TRACKING EVIDENCE FROM A VISUAL SEARCH TASK

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Long-distance human space travel will lead to communication delays and with increasing distance from earth, support from ground control will be partially replaced by the interaction with automated support systems. To make good and fast decisions, operators need to attend to displays and quickly identify relevant among irrelevant information. We used a visual search paradigm to operationalize such tasks and studied performance under sleep deprivation. Sleep quality and quantity suffer during space missions and prior work has suggested that performance in these tasks becomes «fast and sloppy» with sleep loss. We used eye-tracking to get insight into the underlying processes that lead to this type of poor decision-making.

We studied 50 healthy participants, randomized to a 24-h acute sleep deprivation group and a control group, completing a visual search task in which they had to decide on the presence/absence of a single target within sets of 10, 20, 30 or 40 search

items. Eye-tracking revealed that, across both groups, visual sensitivity correlated positively with total fixation duration (TFD) and with TFD slope, i.e. the rate at which TFD increases as a function of set size. After sleep loss, sensitivity deteriorated more in trials with 30 and 40 items than in trials with 10 and 20 items, whereas TFD increased for the small, but not for the large set sizes. Thus, sleep deprivation resulted in a flatter TFD slope, which was associated with poorer performance. Against a background of general cognitive slowing (longer TFD), sleep loss impedes the allocation of sufficient search time to complete more challenging searches with larger set sizes (shallower TFD slope).

This unfavorable speed-accuracy trade-off might indicate attempts to counteract the effect of sleep loss in simple tasks, which fall short due to compromised effort allocation for more demanding tasks. In consequence, decision quality of operators is most impaired when two stressors meet: high cognitive load and acute sleep loss. Eye-tracking measures are sensitive to sleep deprivation and might reflect impairment or compensatory behavior during critical operations. In scenarios of increased crew autonomy, these unobtrusive measurements could inform about operator state and help predict and prevent performance impairment due to stressors.

ANALYSIS OF BACTERIAL PROFILES OF AGBRESA PARTICIPANTS –A STUDY CONCERNING TERRESTRIAL ASTRONAUTS UNDER SIMULATED MICROGRAVITY

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Introduction. Long-term space missions are accompanied by harmful environmental conditions like microgravity. Due to the reduced gravity, astronauts adapt to their environment resulting in tissue fluidic shifts. Since the knowledge about microbiome data in space is sparse and conduction of experiments at the ISS is complex, suitable analogs are needed. Therefore, the first cooperative bed-rest study called Artificial Gravity Bed-Rest study with ESA (AGBRESA), by NASA, ESA and DLR offered optimal features to investigate possible correlations between microbial shifts and physiological microgravity by using -6° head-down-tilt (HDT). The aim of this survey was to identify changes within the standardized conditions, such as diet and wrongly distributed tissue fluids to reveal causal connections among health state and microbial communities.

Methods. Microbiological tests were performed in both, campaign I and II with each 12 participants. All test subjects experienced a 15-day Baseline Data Collection (BDC), a 60-day Head-Down-Tilt (HDT) and a Recovery (R) of 14 days. In campaign I, at regular intervals swab samples from forehead skin and ears were taken. Physiological skin parameters (pH, hydration level & sebum content) were measured using dermatological probes by Courage+Khazaka. For the analysis of changes in the gut microbiome, stool samples were taken from all test subjects during campaign II. Microbial determination was performed by the isolation of genomic DNA (DNA powersoil Kit, Qiagen), amplification of V4 region of the 16S rRNA gene by PCR and sequencing of the products on Illumina platform.

Results. During HDT the microbial analysis of the skin revealed a significant increase of lipophilic Cutibacteria and Corynebacteria with simultaneous accumulation of sebum and water on forehead skin whereas populations of Acinetobacter sp. decreased. As latter are usually found on dry skin, shifted skin parameters are confirmed, thus indicating an instable skin barrier. Concerning ear infections, Pseudomonas sp. was identified as the responsible pathogen while signatures of Staphylococci, Cutibacteria and Corynebacteria were only observed in the healthy ear. Hence, low abundances of these possibly beneficial genera could initiate the infection process of pseudomonads. After first antibiotic treatment, the pathogenic organism was highly reduced while healthy flora was almost restored to its origin state. Furthermore, the microbiome analysis showed individual compositions on participants' skin.

Conclusions. The evaluation of the stool samples is still pending. To cover all fields of the systems biology, proteomics and metabolomics analyses will be here conducted. In order to maintain astronauts' health and life-saving equipment for future space missions, these first data could help to develop appropriate countermeasures like probiotics or skincare.

SORT-TERM HINDLIMB UNLOADING IMPAIRS DOPAMINERGIC REGULATION IN THE STRIATUM OF MICE

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The basal ganglia, which process and coordinate signals from other parts of the brain, play a significant role in the regulation of motor activity (Lanciego et al., 2012). The striatum is a central part of the basal ganglia, that collects and

processes the information from the substantia nigra, hippocampus, cortex and thalamus. There are two ways by which the striatum induces or suppresses movement. The direct pathway stimulates the motor cortex and movements, but the second, indirect, pathway downregulates motor activity. (Le Moine and Bloch, 1995; Wall et al., 2013). However, the question about the functional state of the striatum during decreased motor activity caused by real or simulated microgravity remains open.

Here we analyzed the striatum of mice after 3 day hindlimb unloading (HU). Firstly, we evaluated the expression and activity of tyrosine hydroxylase (TH), the rate-limited enzyme for dopamine (DA) synthesis. In the striatum TH is localized in the terminals of dopaminergic neurons of the substantia nigra. We observed a decrease in TH expression in the dorsal striatum after 3 day HU that demonstrated attenuation of dopaminergic innervation, but phosphorylation of TH at Ser31 was significantly higher, which indicated the activation of DA synthesis. These data suggest that upregulation of TH activity may compensate its decreased expression and thus mediates adaptation of nigrostriatal system to antiortostatic unloading.

We also showed that short-term HU increased expression of DA receptors D2 (D2R) in the striatum of mice. These receptors are expressed in medium spiny neurons, which participate in the activation of indirect pathway and subsequent inhibition of motor activity. It is known that DA inhibits adenylate cyclase dependent activation of PKA by acting at D2R. Indeed, an increase in D2R expression in the striatum of HU mice was accompanied with inhibition of PKA activity. We supposed that activation of indirect pathway was induced by absence of normal hindlimb locomotion.

Additionally, we analyzed expression of Synaptosomal-Associated Protein 25 (SNAP25) and vesicle-associated membrane protein 2 (VAMP2) - the main components the exocytosis machinery. Obtained results showed a decrease in the expression of SNAP25, while expression of VAMP2 was increased after 3 day HU. The revealed changes in the expression of synaptic proteins probably indicate downregulation of synaptic transmission in the striatum induced by short-term HU.

Thus, our data demonstrate that short-term HU leads to inhibition of dopaminergic regulation of the striatum and activation of indirect pathway of basal ganglia.

ADENOSINE BIOMARKER ALTERATIONS DURING A 60 DAY HEAD DOWN TILT BED-REST STUDY. POTENTIAL ROLE OF REACTIVE SLEDGE COUNTERMEASURE

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Optimum Conservation of cellular and molecular body functions is of crucial importance for long-term space missions and bed-rest study environments including head down tilt bed-rest (HDTBR). In these environments, shifts in many physiological biomarkers have been observed. Among others, adenosine (Ado) might be also altered. Of note, Ado is mostly used as a second messenger and broken down by adenosine deaminase (ADA), which is present in red blood cells and the vessel wall, as Ado reaches the circulation. Despite scientific advances in the field, no HDTBR study has been conducted demonstrating the potential alterations in Ado biomarkers in the presence or nor of reactive sledge (RSL) application.

In the current work, we investigated the alterations of Ado biomarkers through its two enzymes tADA and ADA2 in a microgravity analog environment of HDTBR, as well as the effectiveness of the reactive sledge jump countermeasure to promote Ado physiology.

Twenty-three healthy male volunteers were maintained in 6° head down tilt position for 60 days and assigned either to a control or to a RSL group. Blood collection were performed at data acquisition day 2, 14, 30, 40, 50 and 60 (HDT2, HDT14, HDT30, HDT40, HDT50 and HDT60) and recovery day 1 and 7 (R1 and R7). Immunochemical techniques were employed for Ado enzymes (total adenosine deaminase (tADA) and adenosine deaminase 2 (ADA2)) estimation.

Our findings revealed that tADA & ADA2 biomarkers production is altered in control or RSL group during a two-month of HDTBR conditions, following a certain pattern. Specifically, statistically significant tADA and ADA2 variations were present at all time and specific intervals, respectively, in the control group. Under same experimental conditions, in the RSL group, simulated microgravity effects on seem to be attenuated with less pronounced adenosine biomarkers fluctuations were observed on both tADA and ADA2 biomarkers.

Generally, simulated microgravity conditions affects adenosine physiology while RSL effectiveness as HDTBR countermeasure is demonstrated. This work set a background for potential adenosine clinical role and effective countermeasure in sedentary lifestyle, geriatric and space medicine.

THE ROLE OF MUSCLE TONE IN THE GENES EXPRESSION REGULATION THAT CONTROL THE DESTRUCTION OF CONTRACTILE AND CYTOSKELETAL PROTEINS OF UNLOADED SOLEUS IN RAT

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We investigated the role of soleus muscle tone and decrease in its motor neuron activity in change in the genes expression, breakdown of contractile properties and cytoskeletal during unloading. Tetanus toxin (TTX) administration attenuated the muscle tone decrease. TTX first binds at the presynaptic terminals of the neuromuscular junction and is then transported by motor neurons to the spinal cord. TTX action is based on the blocking of GABA and glycine release from nerve endings by cleaving synaptobrevin (Schiavo et al., 1992) that leads to a long-term increase in muscle activity that cannot be achieved with any electrical muscle stimulation protocol. TTX administration into the systemic circulation results in widespread continuous involuntary contractions, known clinically as «generalized tetanus». However, targeted administration of limited amounts of TTX can lead to greater excitation of local muscles only (a result known as «focal tetanus»). We did a 7-day experiment. Wistar rats were assigned into 4 groups (n = 7 rats per group): intact control (C), the control group treated with TTX injection into soleus (1 ng/ml), once on the first day, (CT); hindlimb suspended group (HS); hindlimb suspended group with TTX injection into soleus (1 ng/ml) (HST group). Soleus dry mass of HS rats was significantly decreased (by 50 %, $p < 0.05$) vs C. HS led to a decrease in soleus single contraction strength (by 38 %, $p < 0.05$) vs C group (but not in CT and HST). The isometric tetanic contraction strength in the HS group decreased by 65 % ($p < 0.05$) relative to C group, the TTX administration prevented it in HST group. A decrease (by 30 %, $p < 0.05$) in the specific tetanic contraction force (referred to cross-sectional area (CSA)) was observed only in HS, but not in other groups (vs C). Despite the decrease in the cross section of the soleus, we found neither a decrease in the strength of its single contraction, nor in the strength of isometric tetanic contraction in the HST relative to the C group. Desmin content was reduced by 31.4 % ($p < 0.05$) in the HS group relative to the HST group. In all other groups, there were no differences from the control in this parameter. The MuRF-1 and atrogin-1 mRNA level did not differ between HS and HST groups, and significantly exceeded those in groups C and CT (by 100 and 300 %, respectively, $p < 0.05$). The calpain-1 protein level was increased in HS only versus C (by 48 %, $p < 0.05$), but not in other groups. The content of p-p70S6K (T389), a marker of mTORC1 activity, was significantly reduced in the HS group (by 41 %, $p < 0.05$), and this decrease was prevented in rats by TTX administration (HST). The highest phosphorylation of eEF2 at threonine observed in HS (by 77 %, $p < 0.05$) vs C. It was prevented in HST group.

Conclusions. TTX administration into soleus during HS 1. reduces the atrophic changes in it. This occurs due to prevention to a decrease in protein synthesis, but not to changes in markers of the ubiquity-proteasome signaling pathway; 2. prevents a decrease of single contraction strength, a decrease in the passive stiffness of soleus, and a decrease in the strength of isometric tetanic contraction in comparison with HS group; 3. prevents of desmin proteolysis, which may be due to the absence of calpain-1 level increase in soleus in this group.

This work was supported by a grant from the Russian Science Foundation No. 18-15-00062.

DISTINGUISHING FEATURES OF HUMAN ADAPTATION TO LONG-TERM SPACE FLIGHTS ONBOARD OF THE INTERNATIONAL SPACE STATION

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Introduction. Our efforts to find out the main features of human adaptability to space flights (SF) pierce through all 60-year history of manned space activities in cosmonautics and astronautics from the historical start of Yuri Gagarin on April 12, 1961 up to long-term missions on the International Space Station (ISS) at present. Along with a success in common health care during SF the unfavorable effects of microgravity and other factors of long-term SF, particularly, on a human muscular-skeletal system, maintenance of energy balance and body composition even with used countermeasures are still present, and this problem can grow up with the expansion of humanity to assimilate other planets.

Therefore, the main goal of the present research was the disclosure of distinguishing features of human adaptation to long-term SF onboard of the ISS via the detailed analysis of the fulfilled physical exercises, energy balance, and meal intake and body composition of the Russian cosmonauts – participants of experiment «MORZE».

Materials and methods. The fulfillment of physical exercises (PHE) including aerobic and anaerobic loads – active and passive walk and run (PR), squat (ST), heel raise (HR), deadlift (DL), Romanian deadlift (RDL) and their caloric values, body mass (BM), critically important parameters of body composition (BC) – lean body mass (LBM), body fat mass (BFM), body cell mass (BCM), extracellular mass (ECM), dry lean mass (DLM), phase angle (PA) and rest energy expenditure (REE) by

bioelectric impedance analysis and bioelectric impedance vector analysis, meal intake (MI) with absolute and caloric values of proteins, lipids and carbohydrates were determined in 17 Russian male-cosmonauts during SF of 41/42–56/57 ISS missions in 36-88 days (1 stage of SF – 1SF) and in 132–180 days of SF (2 stage of SF – 2SF).

Main results. Absolute means of compartments of BC within SF were not differed compared to pre-flight values, except tendency to decrease of BCM, while the assess of means in %% to initial personal values revealed the significant decreases in BM%, LBM%, BCM%, ECM%, DLM%, PA%, REE%, and increase of BFM% at 1SF and at 2SF comparing to pre-flight period without difference between 1SF and 2SF. There were no difference in PHE and MI between SF stages, except ST (in % to recommended) tendency (1SF>2 SF) at decreased MI during all SF (48–80 % of recommended caloric content, CC %). The comparison of cosmonauts divided into 2 groups due to their strategies of adaptation to SF (S1 and S2) have revealed the significant differences in LBM, LBM %, BCM, BCM %, ECM %, DLM %, PA %, REE, REE % (S2 > S1), and in PR, ST, HR, DL, RDL, BFM, and BFM % (S2 < S1) with practically equal CC % of MI.

Conclusion. The received results show that S1 practically is the passive «strategy of submission», while S2 is the active "strategy of resistance", which are differed by more adequate i.e. complete (S1) or incomplete (S2) adaptations to microgravity with the losses (S1) even with increased use of countermeasures, or preservation and/or minimization of losses (S2) of the basic structures of organism (except BFM loss in S2). S2 was specified as «gravity-oriented orthograde-determined adaptation – GOODA» (I.A. Nichiporuk, 2016, 2019; I.A. Nichiporuk et al. 2019). The strategy of GOODA looks preferable, especially, in the cases of necessity to work in orthograde position just after acute changed environment like "long-term microgravity – gravity".

INTERRELATION OF SUCCESS IN ADAPTATION TO CONDITIONS OF SPACE FLIGHTS WITH INITIAL BIOCHEMICAL AND NEUROHORMONAL STATUS OF COSMONAUTS

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Introduction. The prediction of success in adaptation to conditions of space flights (SF) is an attractive problem of the modern space medicine as its realization can help to minimize even to avoid various adverse effects of microgravity and other factors of long-term human stay on orbit on International Space Station (ISS) or within missions to other planets. This prediction, particularly, is highly attractive if it can be done just in the period of selection of candidates to crewmembers which would be less susceptible to adverse effects of microgravity.

Therefore, the main goal of the present research was a prediction of success in adaptation to conditions of SF by comparative analysis of initial parameters of biochemical and neurohormonal status of cosmonauts with their levels of adaptability assessed after missions on ISS.

Materials and methods. Ranging of adaptability of Russian cosmonauts - participants of our experiments «Diurez», «Biotest», «Sprut-K», «Sprut-2», «Immuno» and «MORZE» was done using two levels «low» (1) and «high» (2) based on results of fluid shifts and body compositions before, during and after long-term SF. Their biochemical and neurohormonal parameters in blood during pre-flight clinical observations were included as independent variables in multiple regression analysis where dependent variable was range of adaptability to SF.

Main results. The results of our space experiments, especially, «MORZE» have given the evidence that cosmonauts had used two different strategies in long-term SF – the passive "strategy of submission» (=strategy of losses) realized through more adequate (complete) adaptation to microgravity with the development of its adverse effects, and the active «strategy of resistance» realized through incomplete adaptation to microgravity with preservation and/or minimization of losses of the basic structures of organism which was specified as «gravity-oriented orthograde-determined adaptation – GOODA» (I.A. Nichiporuk, 2017, 2019; I.A. Nichiporuk et al. 2019). The results of multiple regression analysis of biochemical and neurohormonal parameters in blood of cosmonauts – participants of above named experiments have shown that adherents of GOODA comparing to followers of «strategy of submission» had higher levels of piruvate, alkaline phosphatase with its bone isoform, glutamyltranspeptidase, high density lipoproteins, lipase, creatine-phosphokinase MM isoform, triglycerides, glucose, osteocalcin, and lower concentrations of Mg, Fe, prostatic acid phosphatase, thrombin time and antispermal IgG. It should be noted that all determined parameters were within normal physiological range, and coefficients of multiple correlation and determination were more than 0,999 with standard error of estimate less 0,0001 ($p < 0,0001$).

Conclusion. The received results are characterized like good and comparatively simple and inexpensive preferable pattern which can be useful in practical prognostic use, but these studies, undoubtedly, should be continued including spread-out, corroboration and addition by other scientific data obtained in missions on ISS, perhaps in …omics area.

STRICT HEAD DOWN TILT (HDT) BED REST: THE IMPROVEMENT OF A GROUND-BASED MICROGRAVITY ANALOGUE FOR SANS-RELATED RESEARCH

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HDT bed rest studies conducted in a highly standardized manner have been proven useful in developing and testing countermeasures for the negative effects of zero-g. Unlike in microgravity where all hydrostatic gradients are abolished, a gravitational vector is still present in HDT bed rest. Nevertheless, HDT bed rest reproduces musculoskeletal and cardiopulmonary deconditioning. Yet, earlier 6° HDT-studies have not reproduced cerebral or ophthalmological changes in astronauts, the so-called spaceflight-associated neuro-ocular syndrome (SANS). Apparently, 6° HDT as applied in the past did not create headward fluid shifts mimicking true microgravity conditions. In recent studies, we modified bed rest to a stricter version to improve the model especially for SANS-related research.

Strict HDT bed rest means, that no pillows are permitted during the HDT-phase except for a thin pillow when subjects are lying on their sides. Subjects are camera-monitored 24 h per day and feedback on head resp. upper body position is provided during waking hours, whenever needed.

Since 2017 two bed rest studies were conducted at the DLR Institute of Aerospace Medicine in Cologne. The first project using the strict bed rest condition was the VaPER- (VIIP and Psychological: envihab Research) Study, a 30-day bed rest study with hypercapnic atmosphere – a joint project between NASA and DLR. This was followed by the AGBRESA-Study (Artificial Gravity Bed Rest Study with ESA), this time a collaboration between NASA, ESA and DLR. 60 days in strict HDT were performed to investigate the effects of a short-arm human centrifuge as a comprehensive countermeasure.

Test subjects of both studies showed an excellent adherence and maintained strict 6° HDT throughout the bed rest phases. As a result, we observe an increased cephalad fluid shift indicated by development of puffy faces. Moreover, Laurie et al. observed thickened retinal nerve fiber layer measured via OCT (optical coherence tomography) in both VaPER (increased CO2 + strict BR, 5 of 11 test subjects, ~45 %) and AGBRESA studies (strict BR + AG, 9 of 24 test subjects, ~38 %).

Overall, these findings suggest that strict HDT bedrest reproduces cephalad fluid shifts and SANS-like changes and can now be applied to assess potential countermeasures in a systematic fashion. Indeed, the next NASA-DLR Bedrest Studies (SANS-CM-Studies) planned between 2021 and 2023 will focus on this topic. Different countermeasures will be tested, always in the strict head-down tilt position.

THE MOTILITY OF SPERMATOZOA OF MICE AND *DROSOPHILA MELANOGASTER* CHANGES DIFFERENTLY UNDER MODELLING MICROGRAVITY CONDITIONS

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Human exploration of deep space and its preservation as a species is impossible without solving the problem of maintaining the health of the reproductive system. One of the particular issues that requires research and solution is the motor activity of spermatozoa, which is necessary for fertilization in vivo. Despite the fact that evolution took place under constant gravity, the motility of spermatozoa of different species under microgravity conditions changes in different ways. The aim of this work was to search for a possible mechanism providing a different pattern of sperm motility of mice and *Drosophila melanogaster* under simulated microgravity. Fly and mouse spermatozoa were isolated, exposed for 6 hours on a random positioning machine and evaluated for motility. Sodium fluoride was used to inhibit serine / threonine phosphatases, sodium orthovanadate – for tyrosine phosphatases, and 6-dimethylaminopurine – for protein kinases. All the experimental procedures were approved by the Commission on Biomedical Ethics of the Institute of Biomedical Problems (IBMP), the State Scientific Center of the Russian Federation (Minutes No. 521 dated September 25, 2019).

After a 6-hour exposure to simulated microgravity, the locomotor activity of *Drosophila melanogaster* spermatozoa increased. The addition of a protein kinase inhibitor after exposure did not decrease movement speed. However, the addition of an inhibitor of tyrosine phosphatases leads to a complete cessation of movement both in control and after exposure to simulated microgravity, which may indicate that dephosphorylation of Tyr is an absolutely necessary condition for mobility under any conditions. The introduction of an inhibitor of Ser / Thr phosphatases does not change the speed of movement in the control, however, it neutralizes the effect of an increase in speed after being in simulated microgravity. Therefore, it can be assumed that an increase in the speed of movement under microgravity conditions occurs due to a decrease in the level of phosphorylation of Ser / Thr residues as a result of an increase in the corresponding phosphatase activity. The lack of effect in the control group suggests that this phosphatase activity is not constitutive, but facultative and is activated under simulated microgravity.

On the contrary, in mice, after a 6-hour exposure to simulated microgravity, the motor activity of spermatozoa decreased. The addition of a protein kinase inhibitor after exposure reduced the speed of movement in the control, but did not affect the

speed of movement after simulated microgravity. Accordingly, it can be assumed that under simulated microgravity conditions, phosphorylation increases due to an increase in constitutive protein kinase activity. Moreover, it is likely that this is phosphorylation at Ser / Thr, since inhibition of their dephosphorylation also leads to a decrease in the speed of movement in the control. In this case, dephosphorylation of Tyr residues, in contrast to *Drosophila melanogaster*, is not a necessary condition for sperm motility.

This work was financially supported by the program for fundamental research SSC RF – IBMP RAS 65.4 and Strategic Academic Leadership Program.

THE EUROPEAN SPACE AGENCY'S HUMAN RESEARCH ACTIVITIES: PAST, PRESENT AND FUTURE

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The European Space Agency (ESA) has a longstanding history for enabling fundamental and applied research in the areas of human research, both on Earth and in space. More specifically, ESA is supporting topical teams and research activities in bedrest studies, isolation and confinement environments (including the Concordia station at Antarctica and the SIRIUS missions in the NEK ground-based facility at IBMP), parabolic flights and the International Space Station. With the end of lifetime of ISS approaching, all space agencies are preparing to move beyond low earth orbit (LEO) and onwards to Lunar vicinity and orbit, Lunar surface and eventually Martian missions.

Consequently, these missions pose great challenges for the human body, such as an altered gravitational environment, radiation, and isolation and confinement. In order to prepare astronauts as good as possible and apply effective risk mitigation, these risks and their impact on the human body are to be better understood. We aim to give a full overview of ESA's past, present and future human research activities in this area. In particular, we will focus on the future in which ESA is aiming to not only build upon the current research platform portfolio, but to further expand it with ESA-sponsored dry immersion and isolation and confinement studies. Opportunities for the scientific community to get involved will also be addressed.

ARFA-19 EXPERIMENT: SIMULATION OF THE MAGNETIC FIELD UNDER EXPOSURE CONDITIONS

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The article presents data on an experimental study of the influence of a hypomagnetic environment on the electrophysiological characteristics of the myocardium and their relationship with the processes of autonomic regulation of blood circulation in the framework of the addition to the SIRIUS 2018\2019 program – «Arfa-19», section modeling of magnetic fields at the «Arfa» base bench.

According to the study cyclorama, each test subject (8 volunteers in the «Arfa-19» research program) participated in three exposures – 3 exposure days, ATD (adaptation-training day), exposure duration 300 min; placebo and hypomagnetic conditions (HMU) with an exposure time of 540 minutes. During exposures to ATD and placebo, the background values of the magnetic field were recorded. In all expositions, external magnetic conditions were controlled according to data from the Moscow Observatory with local coordinates: 55.48 degrees north latitude and 37.31 degrees east longitude. According to these data, all experimental days – placebo and HMU, with the exception of 1 day, passed in conditions of a calm or weakly disturbed geomagnetic field.

For the entire group of testers, the average value of the magnetic field in the «Arfa» installation during the Placebo exposure was 46.32 ± 0.38 μT, and when exposed to hypomagnetic conditions, 0.044 ± 0.010 μT, which corresponds to the average multiplicity of weakening of the local geomagnetic field 1053 in the group range from 872 to 1296.

Thus, the «Arfa» facility made it possible to technically provide research on the influence of hypomagnetic conditions on the physiological parameters of the human body during long-term exposure.

PERIPHERAL COOLING IN THE HUMAN SHORT ARM CENTRIFUGE CAN REDUCE ORTHOSTATIC INTOLERANCE

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Orthostatic dysregulation is a well-known possible phenomenon when leaving microgravity and returning to +1g. External peripheral cooling has recently been described as a potent countermeasure during heat stress and in lower body negative pressure apparatus. We therefore hypothesized that such cooling may also be effective in hypergravity situations. To do this, we designed a randomized, controlled short-arm human centrifuge experiment («Coolspin») with a crossover protocol to investigate if peripheral cooling can act as a stabilizing factor in cardiovascular functioning.

18 healthy male volunteers completed two runs in the centrifuge and afterwards performed a physicalexertion teston an ergometer. Higher blood pressure values were analyzed when comparing the cooling protocol to the non-cooling protocol. Electrocardiography revealed an increasing heart rate during the run with a tendency towards lower values in the cooling protocol group. Regardingthe stroke volume, total peripheral resistance and cardiac output no differences were observed. In terms to time to failure,catecholamines,maximal oxygen consumption, and maximal workload, no differences were found. Ourexperiment shows that cooling could be a promising countermeasure to combat orthostatic intolerance when transitioning to higher g forces.

ACCURACY OF POWER MAINTENANCE BY MUSCLES OF THE SHOULDER GIRDLE AFTER 21-DAY DRY IMMERSION

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We compared the ability to maintain a given power when performing complex-coordinated movements by the shoulder girdle muscles in untrained volunteers (before and after staying in a 3-week «dry» immersion) and in athletes training endurance (skiers before and after a three-month period of intense training). Athletes and untrained volunteers were tested on a ski arm ergometer with a stepwise increasing load till exhaustion. The anaerobic threshold was assessed and the accuracy of maintaining the power was estimated by the standard deviation of the performed load from the given one. In both groups the accuracy of maintaining a given power of movements gradually decreased as the load increased. 21-day of «dry» immersion was accompanied by a slight decrease in the anaerobic threshold, however, there was no change in the accuracy of maintaining the power of movements during complex-coordinated work of the shoulder girdle. This could be associated with the fact that immersion affects mostly the motor units responsible for maintaining posture. 3-month training of athletes led to an increase in the anaerobic threshold from 107 ± 32 to 177 ± 44 W. An increase in fitness did not influence the absolute error on the load, however, it led to a noticeable decrease in the relative error: in the load range 30 % to 80 % of the maximum power, it decreased from 4.7 % ± 0.3 % to 3.4 % ± 0.1 %/by 28 %.

The work is performed according to the Plan for Fundamental research #64.1 of SRC RF Institute of Biomedical Problems RAS.

GREEN MOON PROJECT: ENCAPSULATED AND PRESSURISED HABITAT FOR PLANTS ON THE MOON (HABITABILITY AND SPACE AGRICULTURE)

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With multiple human space missions projected to nearby planetary bodies for the next few years, humanity will become an interplanetary species and must be sustainable. Humans traveling to the Moon, Mars, as well as other planetary bodies will have to grow plants for food. In this way, they will be able to reduce the weight of their trip by being able to use in situ resources (ISRU). The cultivation will allow to take the first step to establish the future human bases on the lunar or Martian surface; it is a need that will make these missions sustainable.

Understanding how the growth of plants would be like under the conditions of gravity and radiation that can be found on the Moon is essential before starting to establish future human there. In addition to generating food for the astronauts, thanks to the photosynthesis carried out by plants, they will reduce carbon dioxide and they will generate oxygen.

Green Moon Project combines planetary geology, plant biology and aerospace engineering in order to know everything necessary to support space agriculture, as well as the habitability of future manned missions to the Moon or Mars. In this way, the lava tubes are very important in the project as they help protect from cosmic radiation. For this reason, the island of Lanzarote, of volcanic origin, becomes a natural laboratory where to test with rocky substrate similar to the one that which could be found on the Moon or Mars. From a plant biological perspective, horticultural crops are essential as they provide

nutrients, as well as vitamins to humans who travel to the Moon, Mars and beyond. The component of aerospace engineering is seen in the capsule or small space greenhouse within which the cultivation takes place.

The encapsulated instrument where the crop will take place (in a first phase) will be made of a series of sensors for carbon dioxide, oxygen, humidity, luminosity, temperature, radiation, as well as a multispectral camera to take images; the germination of the seed and subsequent growth of the plant stem. Green Moon Project has the support of the Spanish Network of Planetology and Astrobiology (REDESPA), the Institute of Geosciences of Spain (IGEO), the Cabildo de Lanzarote, as well as the UNESCO Geopark of Lanzarote. In September 2019, Green Moon Project signed a collaboration agreement with the Chinese Center of Space Exploration (COSE) of Chongqing University, the same group that managed to plant the first cotton plant on the Moon in January 2019.

FUNCTIONAL CONDITION OF THE VISUAL SYSTEM UNDER THE CONDITION OF ONE-YEAR WINTERING AT THE ANTACRTIC STATION VOSTOK

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One of the most important tasks of medical support for space flights and missions that involve locating on bases on other planets is the prediction and prevention of functional disorders of the central nervous system in extreme conditions.

Antarctica is considered as a ground-based model of the effect of space factors on the functional stability of a human. Such habitat conditions for polar explorers at Vostok station in Antarctica, such as unstable electromagnetic background, hypobaric hypoxia, hypodynamia, isolation in a confined space, artificial lighting are in many ways similar to the factors of the artificial habitat of a spacecraft or on a base on another planet, and this makes it possible to use the functional stability of the human CNS as applied to the problems of medical service of deep space flights. For the first time, our institute has carried out comprehensive studies of the state of the human visual sensory system during a one-year wintering at Vostok station.

The aim was to obtain new objective data on the study of the functional stability of the visual sensory system at various stages of a year's stay in extreme conditions and to test telemedicine technologies for monitoring the fundus vascular system in expeditionary conditions.

The study involved 9 male polar expeditioners aged from 33 to 65 years, with visual acuity of 0.9–1.0 with correction. The monitoring of the functional state of the visual system included morphometric assessment of the fundus using a Smartscope-m5 portable digital fundus camera, daily dynamics of intraocular pressure using an Icare PRO tonometer (TA03), assessment of the secretory activity of the lacrimal gland (Schirmer's test). Psychophysiological visual functions were assessed in terms of spatial contrast sensitivity, lability of the optic nerve (CFFF), Bourdon's correction test.

The analysis of the fundus state revealed a high adaptive ability of the mechanisms of autoregulation of blood circulation in the posterior pole of the eye and apparently as a consequence the preservation of trophic autorgelation of cerebral vessels, which is triggered even with a slight decrease in tissue oxygen saturation and an increase in pH. A comprehensive assessment made it possible to conduct a correlation analysis of the levels of functional stability of the eye circulatory system, intraocular pressure and visual performance in general during prolonged exposure to extreme conditions.

RESISTANCE MECHANISMS OF BACILLUS SUBTILIS-20 AND BACILLUS LICHENIFORMIS-24 STRAINS

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Introduction. Space with its extreme conditions (extreme temperature differences, solar and galactic radiation, vacuum, hypomagnetic field, etc.) is absolutely unsuitable for the life of living organisms. Inside the International space station, conditions are maintained to reduce or eliminate the space factors influence to allow astronauts to carry out space missions. Such conditions are more or less suitable for the existence of some microorganisms: molds and bacteria. The increased level of ionizing and other types of radiation and the accumulation of reactive oxygen species serve as damaging factors to microbial cells' hereditary material due to the International space station's conditions. For most types of prokaryotes, these factors are devastating. It seems to be the cause of the depleted biodiversity of microorganisms identified at space stations. However, spore-forming bacteria can survive on the International space station, apparently due to the development of new mechanisms for resistance to DNA-damaging factors. To date, little is known about the mechanisms of adaptation of microorganisms to the destructive conditions of outer space and, in particular, to DNA-damaging factors.

Object. The research aims to study the molecular mechanisms of *Bacillus subtilis-20* and *Bacillus licheniformis-24* strains resistance to DNA damaging factors of outer space.

Materials and methods. The comparison strains were *Bacillus subtilis-168* and *Bacillus licheniformis-B10956* from the All-Russian Collection of Industrial Microorganisms. *Bacillus subtilis-20* and *Bacillus licheniformis-24* strains isolated from internal International space station volumes were used.

We used methods for mass spectrometry analysis, ribosomal DNA sequencing, analysis of bacterial growth kinetics, determination of hydrogen sulfide production, measurement of gene expression levels, and suppression of gene expression using a CRISPR/dCas9 system.

Results and discussion. We find that *Bacillus subtilis-20* and *Bacillus licheniformis-24* strains are more resistant to some DNA-damaging agents: UV, zeocin, 4-NQO, and MMS. Hyper-resistance to DNA-damaging factors of the studied strains is associated with over-expression of the NHEJ-system for double-stranded DNA breaks repair. The crucial role of the NHEJ repair system was confirmed in an experiment of suppression of the expression of the NHEJ system genes by CRISPR/dCas9 upon conditions of DNA damage caused by the antibiotic zeocin. The analysed strains show hyper-resistances to hydrogen peroxide. In the case of *Bacillus subtilis-20*, it may be due to over-expression of the katA catalase gene and increased hydrogen sulfide production, which is involved in the neutralization of reactive oxygen species. At the same time, *Bacillus licheniformis-24* produces less hydrogen sulfide than *Bacillus licheniformis-B10956.* But over-expression of catalases and superoxide dismutases has been determined.

The findings show the enzymatic antioxidant protection systems are of greater importance in the over-resistance of the *Bacillus licheniformis-24* strain to oxidative stress.

Conclusion. The obtained information will help to plan long-term space expeditions to other planets by developing adequate measures to control microbial activity, taking into account their resistance to stress impact.

RADIOBIOLOGY OF EYE

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The eye is a unique organ because it is constantly exposed to radiation and atmospheric oxygen. This combination of radiation and oxygen is extremely dangerous for the development of oxidative stress. Radiation-induced cell damage involves generation of reactive oxygen species in the cell. Free radical-induced ocular tissue damage has been associated with a variety of pathological conditions. Oxidative stress is likely to be involved in the pathogenesis of UV- and radiation-induced cataract and retinal damage.

Visible light is a natural solar radiation that has formed the eye in the course of evolution and which initiates the physiological process of vision. The adverse effects of UV and ionizing radiation on the eye, first of all lens and retina, have been reported by multiple investigators. A unique feature of the space radiation environment is the presence of high-charge high-energy particles of the galactic cosmic ray environment and proton-rich solar particle events.

The retina consists of terminally differentiated cells that have lost their ability to proliferate. The retina is characterized by relatively high resistance to radiation, which is provided by its ability to repair damage caused by ionizing radiation [Tronov V.A. et al., 2012; Vinogradova Iu.V. et al., 2014].

Ionizing radiation leads to radiation oxidation in the tissues of the eye. For example, radiation by accelerated protons or gamma radiation of bisretinoids accumulating in the retina and retinal pigment epithelium cells leads to the formation of their toxic oxidized forms [Yakovleva M.A. et al., 2019].

The lens of the eye is among the most sensitive organs to ionizing radiation. International Commission on Radiological Protection (ICRP) reduce dose threshold for cataract induction to 0.5 Gy. We have proposed a molecular mechanism that may underlie the appearance of any lens opacity, including UV and ionizing radiation induced [Muranov K.O. and Ostrovsky M.A., 2013; Muranov K.O. et al., 2019]. Various cataractogenic factors (aging, various types of radiation, high blood sugar levels) that damage the lens facilitate the penetration of oxygen into it. The increased oxygen levels, combined with radiation, damage the lens proteins crystallins, which begin to aggregate. As a result, the lens becomes cloudy, that is, a cataract is formed.

PROMISING RESEARCH AREAS FOR THE OPERATIONAL CONTROL OVER THE HUMAN HEALTH TOXIC RISKS IN LONG-TERM MANNED SPACE FLIGHTS

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The lengthening of orbital expeditions and interplanetary missions in the future, make it necessary to develop a system for the operational control over the human health toxic risks in long-term manned space flights. Currently, the criteria for toxic

risk assessment are based on the hygienic standards (PDK) of the isolated exposure to trace contaminants. It is insufficient due to the peculiarities of the physiological and mental adaptation of cosmonauts in long-term manned space flights. The way to solve the problem is to establish the hygienic standards, adjusted by coefficients, which take into account the combined exposure to the main negative factors.

A systematic analysis of air pollution onboard the spacecrafts allowed us to set the main factors affecting the toxic process. Nowadays, the research areas that require priority solutions are:

1. Experimental rationale of quantitative contribution for each of the main negative environmental factors, such are: long-term and continuous exposure to the multicomponent chemical air pollution and ionizing gamma radiation in zero gravity;
2. Study of chemical toxicokinetics (in case of the fluid shift in cranial direction) during a space flight;
3. Study of toxic effects (additive and/or potentiating synergism) caused by the combined exposure of the main unfavorable spaceflight factors and mixture of air toxicants typical for space stations.

The study of bioeffects caused by isolated and combined exposure of the main spaceflight factors in a series of experiments with laboratory animals made it possible to determine the promising research areas which are necessary for the development of methodology and criteria for toxic risks assessment:

1. Experimental rationale and development of a mathematical model for quantitative health risk assessment under nominal air pollution conditions onboard the space stations, as well as in case of emergency situations.
2. Experimental rationale and development of mathematical models for rapid calculation of hygienic standards with different periods of average concentrations (hourly, daily, monthly etc.).
3. Hygienic standardization for allowable carbon dioxide concentrations during a long-term space flight.

The basis for the accelerated establishing of hygienic standards with different periods of averaging will be substantiated and adapted into practice using mathematical models for calculation of the hygienic standards of chemicals (including the equations which are taking into account the hazard class and toxicological end points of chemicals).

Currently, absence of carbon dioxide standards with different periods of averaging stresses the need for the experimental rationale of permissible concentration for carbon dioxide in the air of the long-term space stations. The solution will require experimental verification of the physiological effects of prolonged exposure to the moderately increased carbon dioxide concentrations. It should be noted that due to the increasing amount of newly constructed high-rise residential buildings with insufficient ventilation, double window packages and sealed doors, the carbon dioxide standards are also a subject of study for hygienists working in the area of environmental sanitation.

THE RATIONALE OF THE KEY TRACE CONTAMINANTS LIST FOR CHEMICALS, POLLUTING THE AIR OF MANNED SPACECRAFT

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Systematic analysis of the ISS air chemical composition during 18 years of air quality monitoring showed the expansion of the range of hygienically significant trace contaminants with a shift towards an increase in the proportion of highly and moderately hazardous chemicals for which standards should be established to assess human health risk during the long-term orbital and interplanetary space flights. Currently, due to the technical capabilities of the analytical equipment, there is no way to conduct online analysis of human health toxicological risk assessment for all of 221 detected chemicals which have different physical and chemical properties. On the other hand, in flight human health risk assessment from the simultaneous inhalation of a broad number of potentially harmful chemical compounds with different toxicity will require a huge research, which is impractical due to the constant increase in newly identified chemicals during a long-term space flight.

In this regard and following the provisions of Guidelines 2.1.10.1920-04 «Human Health Risk Assessment from Environmental Chemicals», the studies have been conducted to identify the key trace contaminants list for chemicals, detected in the ISS air, that have a toxicological hazard to health of cosmonauts during a space flight.

The study has included two stages. At the first stage, all of the 221 detected trace contaminants have been ranked depending on the contribution of each chemical to the total air pollution, its hazard class, the frequency of exceeding the standard, maximum concentrations, the possibility of chemical transformation etc.

The second stage has included a human health risk assessment for the inhalation pathway of the harmful chemical compounds. The toxicological assessment has been carried out in accordance with the air quality criteria that are set for the manned space stations. These criteria take into account the specific factors of the system «astronaut's health – habitat» that reduce the resistance of a human to toxic effects caused by the long-term combined exposure to toxicants, different pathways, weightlessness and isolated environment.

The toxicological assessment of the detected chemical compounds includes:
– assessment of the toxicity for each identified substance and calculation of the hazard index HI;
– calculation of the total value $\sum T=\sum_i C_i/PDK_i$ for substances with unidirectional bioeffect and hazard factor value (HQ);
– assessment of the combined exposure to xenobiotics.

Based on the obtained results, the key trace contaminants list has been established. The contribution of these chemicals to the ISS total air pollution is 86.3 %. The contribution of other volatile organic compounds to the total air pollution ranged from 0.001 to 0.6 %, and in total 13.7 %.

The practical significance of the study is determined by the establishment of key trace contaminants list for chemical compounds which are mandatory for monitoring in the multicomponent air of manned spacecraft. The toxicity risk integral indicators have been justified. It has formed the basis for the development of operational and predictive management for human health risks assessment in real time mode to provide toxicological and hygienic safety of air during the long-term space flights.

HUMAN-SYSTEMS INTEGRATION NEEDS ANALYSIS FOR ON-BOARD ANOMALY RESOLUTION DURING EARTH INDEPENDENT OPERATIONS

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Future deep space exploration missions will require small crews to act with greater autonomy than in present or past missions. Limited communications (e.g., bandwidth, latency, etc.), lean sparing and re-supply, and delayed evacuation opportunities all reduce the level and speed of ground support. In times of safety critical operations –especially when anomalies or off-nominal conditions occur—the crew will have to independently and adequately respond to avert potentially severe outcomes. It will not always be sufficient or even possible to 'safe the system' and then wait upon ground intervention.

A Human-Systems Integration Architecture (HSIA) is a construct to describe the communication, coordination, and cooperation between humans and cyber-physical systems that must occur in order to accomplish an operation or mission, including managing critical events. The current HSIA for the ISS is ground-based and manpower-intensive, relying on many engineers and operators with broad and deep expertise; large, distributed datasets; and expansive analytical and computing power. While successful for near earth exploration, this model is not viable for long-term missions to the moon and beyond. The challenge then is how to engineer the future HSIA to marshal the required expertise, data, and computation for the small flight crew to enable them to perform the job that has traditionally been done by a much larger and well-equipped ground crew. This will require a fundamental rethinking of crew-vehicle integration, on-board problem-solving and decision-making, and crew-ground asynchronous collaboration.

The first step toward defining the next architecture is a needs analysis. Our research task is focused specifically on anomaly response – identifying requirements to enable on-board problem detection, diagnosis, resolution, and contingency management. To inform this work, we conducted systematic analyses of ISS system malfunctions and off-nominal operations as well as malfunctions that occurred during the Apollo Missions. We also observed (remotely) the investigations and deliberations of the ISS Mission Evaluation Room and Anomaly Resolution Teams in real-time; interviewed astronauts, flight controllers and instructors; reviewed flight and operation logs; and examined troubleshooting approaches taken in analogous domains.

This will provide a deeper understanding of how urgent diagnosis and resolution are currently done and what products are used to aid the process. The outcome of this task is a set of information and knowledge requirements critical to resolving potentially safety-critical anomalies and a breakdown of how the HFBP disciplines (HCI, TRAIN, HARI, and MPTASK) contribute to the provision of them in the design of onboard systems. Ultimately this information will enable prioritization of the data and expertise needed on-board to support the crew in performing anomaly investigation and sense-making in isolation.

The current presentation will review the IFI database to show 67 high priority IFIs from 2002 to 2019. 35 of the 67 are associated with malfunctions in vehicle subsystems, including active thermal control (ATCS), electrical power (EPS), environmental control and life support (ECLSS), guidance, navigation and control (GNC), and structures (S&M) subsystems. A systematic characterization and discussion of the types of anomalies that occur will also be included in this presentation.

THE ROLE OF HISTONE DEACETYLASE 4 IN THE REGULATION OF SLOW MYOSIN EXPRESSION AT THE EARLY STAGE OF GRAVITATIONAL UNLOADING IN THE RAT SOLEUS MUSCLE

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Gravitational unloading leads to a slow-to-fast shift in the myosin phenotype. The reason for these changes is a decrease in the expression of the genes encoding heavy chains of myosin (MyHC) of the slow type, and an increase in the expression of the genes encoding MyHC of the fast types. Signal cascades such as HDAC4/MEF-2D is known to regulate MyHC I gene

expression. There is almost no data in the literature about HDAC4/MEF-2D signaling regulation involved in the regulation of the gene expression of MyHC I in the rat soleus muscle under the gravitational unloading. The aim of this study was to explore the role of HDAC4 in the regulation of the gene expression of MyHC I in the rat soleus muscle under the gravitational unloading.

Three-month-old male Wistar rats weighing 180–225 g were randomly assigned to four groups (8 animals in each): vivarium control group, vivarium control group+ a HDAC4 inhibitor (Tasquinimod), hindlimb suspended group for 1 day (HS), hindlimb suspended group for 1 day with the introduction of a HDAC4 inhibitor (Tasquinimod) at a concentration of 10 mg/kg body weight per day orally (T).

As a result of 1-day hindlimb suspension, there was a significant increase of nuclear HDAC4 by 374 %, MRF4 by 145 % (immunoblotting) as well as a significant decrease in the expression of pre-Myh7 by 60 % (PCR-RT method) relative to the control group and in the group with a HDAC4 inhibitor (Tasquinimod) no significant differences from the control group were found. Also, there was a significant increase in the expression of pre-Myh7 by 30 % relative to the HS group.

Thus, inhibition of HDAC4 activity at an early stage of gravitational unloading partially prevents a decrease in the expression of slow myosin.

This work was supported by the Russian Science Foundation (RSF) grant # 18-15-00107.

DYNAMICS OF HUMAN VENTILATION RESPONSE DURING 21-DAY «DRY» IMMERSION

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It is known that microgravity and the reproduction of its effects in ground-based experimental models, for example, during «dry» immersion (DI), have a significant effect on the human cardiorespiratory system.

The aim of the study was to experimentally determine the effect of 21-day DI on the reaction of the cardiorespiratory system to an increase of concentration of carbon dioxide (CO_2) in the alveolar gas.

Method. A study of the ventilation response of a person to hypercapnia under DI conditions was carried out in 10 subjects aged 24 to 32 years. During the experiment, the following was measured: 1) ventilation response to hypercapnia by the method of rebreathing into a hyperoxic gas mixture using the Hemosens software and hardware complex developed by us, 2) cerebral blood flow rate by rheoencephalography (REG), 3) lung volumes and transfer factor (K_{DLCO}) by single inhalation method. Measurements were carried out once before the start of DI, on days 4, 8, 13, and 19 during DI, and once on day 4 after the end of DI.

Results and discussion. On the day 4 after DI, a significant ($p < 0.05$ according to the parametric paired Student's t-test) increase by 25 % in the ventilation response to carbon dioxide compared with period before the start of DI was observed. During the DI, the increase of the ventilation response grew, however, it was only the trend. The tidal volume response to CO_2 was significantly higher on days 13 and 19 ($p < 0.05$) of DI compared with response before the start of DI.

Immediately after the start of the DI, all subjects had a decrease in FRC by about one liter. Further, the FRC remained at this level during the DI.

K_{DLCO} statistically significantly decreased during the entire 21-day DI in comparison with K_{DLCO} before the DIand remained reduced on the day 4 after its end.

According to the REG data, a decrease in the rate of cerebral volumetric blood flow during the DI was observed, compared with both «sitting» and «lying» positions, in period before the DI.

Note that the increase in ventilation response to CO_2 found here is comparable with the previously detected increase during the three-day DI [Dyachenko et al., 2015].

Conclusion. An increase in ventilation response to carbon dioxide was revealed during the 21-day DI, which persists and even becomes statistically significant on the day 4 after its end. At the same time, changes in the response of the tidal volume to CO_2 during DI are more pronounced than the dynamics of ventilation response.

THE FUNCTIONAL STATE OF THE HUMAN HEARING SYSTEM AND THE BRAINSTEM ACOUSTIC STRUCTURES IN THE SIMULATED HYPOMAGNETIC FIELD

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The prospects of long-term and interplanetary space missions sets the task of careful selection and higher requirements for the cosmonauts and astronauts health to ensure the manned space flights safety. In this regard, it seems actual to

introduce new neurophysiological methods for the central nervous and auditory system functional assessment into clinical and physiological examination of cosmonauts and astronauts.

The purpose of this study was to estimate the influence of the simulated hypomagnetic field on the functional state of the human hearing system and the brainstem acoustic structures using «ARFA» system.

The experiment involved male volunteers who passed medical selection (n = 8), aged from 27 to 38 years old, average age 33.3 ± 1.3 years, median age 33.5 years.

To estimate of the hearing system functional state, the methods of transient-evoked otoacoustic emission (TEOAE), distortion product otoacoustic emission (DPOAE) and short-latency auditory evoked potentials (SLAEP) were used. The responses to acoustic stimulation of various modality and frequency were recorded. For the TEOAE technique, stimulation with nonlinear clicks in the range from 1 to 5 kHz was used. For the DPOAE technique, stimulation with a pair of pure f1 and f2 tones was used, intensity f1 – 65 dB SPL, f2 – 55 dB SPL in the range from 556 Hz to 4444 Hz. For the SLAEP technique, stimulation with short clicks of 11 Hz frequency were used. For the TEOAE and DPOAE methods, the signal-to-noise ratio (SNR), dB in the frequency band of 500 Hz – 4 kHz were estimated. For the SLAEP technique, the main peak latencies (msec) were estimated.

The nonparametric Wilcoxon test was used to statistically evaluate the significance of the differences between the mean values of the samples. Differences were considered significant at $p < 0.05$.

The studies were carried out in the background («background») and the recovery period («aftereffect»), as well as every 2 hours while the subject was in the hypomagnetic system «ARFA» (HMS) (2 studies on an adaptation-training day («ATD»), and 4 trials each in «placebo» and «HMS» cycles.

Analysis of the obtained data showed a tendency towards a decrease in the OAE signal-to-noise ratio (both TEOAE and DPOAE), mainly in the range of low and medium frequencies during the «ATD» and the «placebo» periods. During the «HMS» period there was a less pronounced decrease in the OAE signal-to-noise ratio in all frequency range and a tendency to increase the OAE signal-to-noise ratio at low frequencies. No significant statistical differences were found. The latencies of the SLAEP peaks were within the physiological normal range.

The otoacoustic emission and short-latency auditory evoked potentials appears to be a promising method for rapid non-invasive assessment of the hearing system and the brainstem acoustic structures functional state in cosmonauts and astronauts in further experiments and in the long-term and interplanetary space missions.

CARDIOVASCULAR DISEASE RISK MODELING FOR ASTRONAUTS: MAKING THE LEAP FROM EARTH TO SPACE

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The risk for radiation-induced cardiovascular disease (CVD) at high doses is well-established from data on clinical, environmental, and occupational exposures. Less is known about CVD risks associated with lower doses, chronic exposures, and from high energy charged ions found both in space and in the clinic. This is a critical area of investigation for occupational radiation protection here on Earth and in space, but it is currently limited by small cohorts and/or small effect sizes that make it difficult to acquire scientifically meaningful results. Elucidating risks from radiation exposure is also complicated by the multifactorial nature of CVD, where traditional risk factors strongly influence an individual's risk profile and can potentially confound analyses, especially at lower doses.

For NASA radiation risk assessment, an integrated framework that incorporates both space radiation exposure and individualized risk factors is desirable. The current NASA model uses excess relative risk and is therefore highly dependent on background rates of CVD incidence and mortality. To consider individual risk factors in the model, a personalized incidence rate, derived from an optimized clinical risk calculator, could replace the current United States population background rates. Many of these baseline CVD risk calculators have been developed with specific sets of risk factors as covariates. For example, the well-known Framingham Risk Score algorithm derives risk of dying from a coronary event over a 10-year period based on individualized risk factors. More recent risk calculators have also included biomarkers like coronary artery calcium and C-reactive protein as additional covariates.

This approach contributes to the refinements in CVD risk assessment needed for astronauts and is a first step in implementing personalized medicine in radiation risk assessment. We discuss information that is needed for an ideal, dual-use CVD risk assessment model that supports both clinical decision-making and operational management of space radiation CVD health risks. Here we review available baseline CVD risk calculators and assess their suitability for use in NASA space radiation applications.

AUTOMATIC PRIMARY MEDICAL DIAGNOSTICS OF COSMONAUTS ON LONG INTERPLANETARY EXPEDITIONS

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Introduction. Since duration of interplanetary space expeditions is growing up, the relevance of primary medical diagnostics carried out by the crew will increase as well. To automate this process, expert systems (ES) can be used to assess how likely disease is present.

The aim of this work was to create and test medical expert system prototype for the primary medical diagnostics to be carried out.

Materials and methods. In the developed ES prototype, we have used rule-based model whose knowledge base currently contains about 270 rules. The model is based on the «Methodological guidelines for operators on the provision of self- and mutual assistance» for Russian segment of the International Space Station. The ES interacts with user through a graphical interface with a speech synthesizer, allowing to indicate complaints and symptoms, as well as objective parameters such as body temperature, heart rate and blood pressure.

Results. Originally indicated complaints and objective status are the initial facts for ES. ES inference engine uses these facts in combination with rules of knowledge base in dialogue with user in order to specify if there are other symptoms corresponding to the identified set of diseases.

The fundamental feature of the proposed approach in comparison with routine selection from the list is that new symptoms (complaints) are presented to the user not by chance, but based on analysis of his previous answers and based on the assessment of how likely new symptom's presence in addition to those already specified.

The result is transmitted as a list of complaints and symptoms to an artificial neural network (ANN), which calculates probability of disease presence depending on the indicated symptoms. An ANN of direct propagation of the «Rosenblatt perceptron» type is used. Now the ANN consists of 112 input layer neurons, which corresponds to the list of symptoms, 300 hidden layer neurons and 81 output layer neurons, which corresponds to the number of diseases that the prototype expert system deals with. To train the ANS, we have used questionnaires filled out by medical professionals, in which they indicated probabilities of symptoms' presence for various diseases.

Discussion. As a result of ANN operation, a list of diseases ranked in accordance with probability of disease presence is formed. This list is compared with the list of diseases generated by the ES. In addition, the level of risk of each disease is taken into account on a five-point scale, the assessment of the probability of the most dangerous conditions can be increased so that further diagnosis begins with them.

Conclusion. The proposed method allows user to obtain a final list of diseases with an indication of the probabilities, from which the least probable diseases are excluded. A further direction of work is the development of a completely speech interface for user interaction with ES and integration with differential diagnosis algorithms, which will clarify the probabilistic list of diseases.

INDIVIDUAL CHARACTERISTICS OF CENTRAL NERVOUS SYSTEM AS AN IMPORTANT FACTOR OF RADIORESISTANCE

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Considering live organisms, most significant factors of interplanetary travel are an impact of high-energy heavy ions, microgravity and hypokinesia. At current technology level none of them can be eliminated, so the only way to make such travel possible is to estimate, how astronauts can withstand these factors. In ground experiments we model irradiation with gamma (1 Gy, body), protons, 12C 450MeV/n and 84Kr 2.3GeV/n ions (0.5–1 Gy, brain). Such doses are about twice higher than estimated doses of Martian Mission, giving us some safety margin. Microgravity is modeled in rats by 7- and 14-days long antiorthostatic suspension, hypokinesia is modeled in monkey by 7-days long antiorthostatic restrain. Key points are to 1) Discover how much these modeled factors affect higher nervous activity (HNA) and 2) Estimate the difference between species with different characteristics of HNA.

In rats we take two groups – more and less excitable according to P.V. Simonov method. In monkeys we use typical temperament graduation, assessing each monkey for strength and balance of nervous processes.

After the impact of modeled factors, rats are tested using conditioned avoidance response (CAR) tests (Y-maze), orientation tests (Morris maze), electroencephalographic recordings and finally brain sampling for concentration of monoamines and metabolites. We discovered, that after irradiation and suspension excitable rats show both faster progress and regress in learning tests, while unexcitable species continuously increase their results without noticeable regress. EEG study shows

significant decrease in frequency and increase of amplitude of delta rhythm as well as decrease in both frequency and amplitude in theta rhythm for irradiated rats. Excitable rats appear to be more affected by model factors.

Monkeys are tested with sophisticated computer software, similar to early computer games, simulating basic elements of operator's performance such as tracking of an object on screen, cursor manipulation by joystick, solving simple geometry and logic tasks like putting cursor in shown area, finding and pointing similar objects. For each successful attempt computer gives monkey a banana grain to stimulate learning, so after several attempts monkey understands basic principles of test and success/fail ratio can be used as a measure of cognitive efficacy.

After impact of modeled factors monkey of balanced type with predominant inhibition shows significant decrease of gaming activity while maintaining good level or successful attempts. Monkey with predominant excitation showed substantial increase of activity combined with low level of successful attempts. Most interesting result is that the monkey of strong balanced type increased success ratio maintaining activity level after an impact of all factors.

To conclude we have to note that: 1) Typological characteristics of HNA have a crucial role in the pattern of neurobiological damages after modeled spaceflight; 2) These damages mostly related to emotional stability and motivation than to cognitive abilities; 3) Strong balanced HNA seems to be the key to individual radioresistance.

THERMONEUTRAL TEMPERATURE MITIGATES HIND-LIMB UNLOADING-INDUCED BONE LOSS BY PRESERVING ENERGETIC METABOLISM

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Hind-Limb Unloading (HLU) induces bone loss in femur and is associated to increased resorption, osteocyte apoptosis and expansion of bone marrow adipose tissue (BMAT). However, most of the HLU studies were performed at housing-temperature below of thermoneutrality in mice, which was evaluated around 30 °C. Therefore, we compared the effects of HLU on bone, at 22 °C, the current standard experimental temperature, to those at 28 °C, a thermoneutral temperature in mice.

Sixteen-week-old male C57BL/6J mice were acclimatized for 4 weeks (1 mouse/cage) and then submitted to HLU or kept, pair-fed with respective HLU mice, in control cages (CONT) for 14 days at either 22 °C or 28 °C (201611231457342-V6, CEEAL-UJM#98). *In vivo* µCT was performed at Days 0 and 14 at femur distal metaphysis. Femora were collected for histomorphometry, osmium-stained bone marrow adipose tissue (BMAT) quantification and multi-staining analysis of osteocyte and lacuno-canalicular networks.

In HLU, body weight and food consumption were respectively lower and higher at 22 °C than at 28 °C. Moreover, HLU22 °C showed 5.6-times lower leptin serum levels and higher BMAT volume compared to CONT22 °C and both 28 °C groups. Trabecular bone loss amplitude was respectively 3.7 and 1.5-times greater in CONT22 °C and HLU22 °C compared to the respective 28 °C groups. Similar results were found in cortical bone. Femur trabecular osteoclastic surfaces (Oc.S/BS, %) were higher at 22 °C (6.6 % and 8.0 % in CONT and HLU) than at 28 °C (2.3 % and 3.9 % in CONT and HLU), respectively. Osteocyte density in femur posterior mid-diaphysis is consistent among unloading and temperature groups (94 966/mm^3 and 99 823/mm^3 in CONT and HLU at 22 °C, 100 842/mm^3 and 98 206/mm^3 in CONT and HLU at 28 °C). Moreover, proportion of empty lacunae is inferior to 0.5 % in all groups. However, significant connectivity alteration was found in osteocyte dendritic processes and lacuno-canalicular network in 22 °C HLU mice compared to respective CONT, but not in 28 °C HLU mice.

VISUAL DWELL TIME ON INSTRUMENTS IS ASSOCIATED WITH MANUAL DOCKING PERFORMANCE

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Manually controlled spacecraft docking on a space station is an operational task that poses high demands on cognitive functioning and visual attention. Effective processing of visual information might be crucial for success. Eye tracking can reveal the operator's attentional focus in an unobtrusive way. Furthermore, the dilation of the pupil has been used as an indicator of task difficulty and mental workload. During docking, this might help to monitor performance and predict decrements due to mental overload. We hypothesized that gaze dwell time on instruments is associated with docking performance and that pupil diameter is associated with the difficulty of the docking task. Eye movements and pupil diameter were recorded in twelve participants (five women and seven men, *M* = 35.5 years old) of the six-degree head-down tilt bed rest study AGBRESA during 20 training

sessions with the *6df* learning program for spacecraft docking. We observed a significant positive relationship between visual checks of speed and distance to the docking point and the accuracy of the docking maneuver. However, pupil dilation turned out to be inappropriate as potential indicator of task difficulty and workload, because it was highly susceptible to differences in screen luminosity. In conclusion, we present first evidence that eye tracking can provide information related to docking accuracy. Future studies are needed to confirm whether performance can indeed be predicted via parameters of visual information sampling.

THE NASA HUMAN RESEARCH PROGRAM: OVERCOMING THE CHALLENGES OF EXPLORATION SPACEFLIGHT

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Humans worldwide are preparing to live and work in space for longer time periods and at destinations deeper into space. NASA's Human Research Program (HRP) takes a risk-based approach to determine the research, technologies and partnerships needed to enable future space exploration.

The NASA Artemis Program will return humans to the vicinity and surface of the Moon. Working in concert with multiple autonomous lander instruments and robotic probes, astronauts will explore the lunar environment and assess the impact of the five main types of space hazards on human health and performance: radiation, isolation and confinement, distance from Earth, altered gravity, and hostile closed environments. Ultimately, the agency plans to use the Moon as a testbed for human exploration of Mars in a «Moon2Mars» initiative.

In partnership with other global and domestic agency, academic, and commercial partners, NASA also uses ground analogs that mimic the space environment and its effects on the human body to fill in knowledge gaps and test countermeasures that moderate risks. Using the international space station as an «ISS4Mars» testbed, NASA can also carry out additional space research needed to prepare for human exploration of the Moon and Mars.

Working collaboratively, NASA HRP's research program crosses discipline, physiological level, species, and platforms to gain the knowledge and tools needed to enable future human exploration of space.

MICROGRAVITY INDUCED RESTING-STATE NETWORKS' AND METABOLIC ALTERATIONS DURING SLEEP ONSET

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The present study focuses on a pipeline involving cortical functional connectivity alterations as a reliable tool for investigating sleep disorders during a microgravity analogue environment. It also investigates the efficacy of the Reactive Sledge Jump (RSL) countermeasure to prevent degradation of sleep after long-term bedrest. For this purpose, cortical resting-state networks during sleep onset (N1) and metabolic blood biomarkers (prolactin and glucose) were analysed after 21 days of head down tilt with the RSL training as a countermeasure. The study involved 23 healthy volunteers who were assigned either to a control or to a sledge group. The data employed were polysomnographic (PSG) recordings through 19 electrode sites, obtained 14 days before bed rest initiation (BDC-14) and 21 days after the initiation of the head down tilt (HDT21). Biomarkers were collected at BDC-1, HDT14 and HDT30 instances. Reconstruction of the cortical resting-state networks was performed by applying generic head anatomy modelling and solution of the inverse problem through the sLORETA methodology. Functional connectivity among the network nodes was obtained with the estimation of the Mutual Information (MI) metric. Significant changes either due to the microgravity (time effect) or due to a group by time interaction were quantified through the Network Based Statistics (NBS) toolbox. Correlations among the brain structures and blood biomarkers were investigated. The results point toward the fact that Head Down Tilt Bed Rest (HDTBR) as a microgravity analogue environment affects both sleep physiology and blood biomarkers, followed by alpha rhythm decreases and a simultaneous increase in prolactin level during sleep onset. On the other hand, there was no consistent result in the correlation between glucose level and alpha rhythm. Our findings highlight a significant degradation of sleep quality during weightlessness which was correlated with blood (prolactin and glucose) biomarkers. However, there were no significant changes regarding the two biomarkers. The lack of evidence for the countermeasure efficacy pinpoints to the need of further research towards the amelioration of the detrimental effect of microgravity.

MORPHOMETRIC STATUS OF THE HUMAN RETINA AS A BIOMARKER OF ADAPTIVE PLASTICITY AND DYSFUNCTIONS OF THE CENTRAL NERVOUS SYSTEM IN CHRONIC STRESS

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Introduction. Chronic stress affects the stability of cell metabolism, which primarily alters the functional activity of the central nervous system (CNS) (Godoy et al., 2018). The main mechanism by which experience-dependent neuronal activity alters brain function is synaptic plasticity (Citri, Malenka, 2008). Prolonged exposure to stress can lead to aberrant changes in brain plasticity that can disrupt its ability to regulate its response to subsequent stressors (Radley, Morrison, 2005). In terms of its metabolic, morphological and functional characteristics, the retina reflects the state of the CNS, which makes it possible to use it as a «window to the brain» in various neuroscience studies. Specific changes in the architecture and function of the retina are biomarkers and predictors of many neurodegenerative diseases (Zueva et al., 2017; Neroev et al., 2020). An urgent direction of scientific research today is the study of early morphometric signs of changes in the retina using technologies of visualization including the optical coherence tomography (OCT). Identification of changes reflecting plastic processes in the retina is important for assessing CNS dysfunction.

Purpose: To assess the efficiency of the morphometric OCT parameters of human retina in identifying signs of adaptive plasticity in psychosomatic manifestations of chronic stress.

Methods. The main group consisted of pilots, men aged 35 to 45 years, with work experience of 10 years or more with psychosomatic manifestations of chronic stress. The age-appropriate control group consisted of persons, whose profession excludes the action of extreme environmental factors. The OCT of the retina was performed using a Cirrus SD-OCT. In the macular region, the morphometric characteristics of the outer retina and the retinal ganglion cell complex, including the inner plexiform layer (IPL), the ganglion cell layer (RGC) and the retinal nerve fiber layer (RNFL) were estimated.

Results and Discussion. In the main group, 38 % of pilots a thickening of the IPL layer was showed, which on average for the group was statistically significant ($p < 0.05$). We associate the increase in the width of the IPL with the adaptive plasticity of the retina, which can manifest itself in the expansion of the dendritic branching of RGCs. These changes are aimed at strengthening functional connections between neurons and ensuring normal processing of visual information sent from the retina to the brain. It is known that chronic stress leads to a decrease in neurogenesis, a violation of synaptic plasticity, a change in the morphology of dendrites (Radley, Morrison, 2005; Joëls et al., 2007) and, accordingly, to a change in the excitability of neurons (de Kloet et al, 2005). In our research, some of the subjects showed a tendency to thinning of the IPL, which may reflect manifestations of maladaptive plasticity. This is the basis for assigning these pilots to the risk group (premorbid state) and the need for their more frequent follow up. It is important to note that diagnostics of the premorbid state is of great importance for the prevention of occupational disorders associated with work under conditions of chronic stress.

Conclusion. The primary analysis of the results indicates that studies of morphometric characteristics of the retina as biomarkers of neuroplastic changes and predictors of changes in the functional state of the central nervous system associated with chronic stress are promising.

IRRADIATION EFFECTS ON THE COGNITIVE TRAIT EXPRESSION AND NEUROGENESIS IN LABORATORY MICE OF DIFFERENT GENOTYPES

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The study presented is the first attempt to evaluate the ability of mice to solve the cognitive problem (elementary reasoning task) after proton, gamma and C12 irradiations. The main part of the study had been performed using male hybrid F1 mice (C57BL x CBA), but males of parental inbred strains were used too. Irradiated mice behavior was compared with that of intact controls and with the group, which was transferred to Dubna and back and was placed there in the irradiation device, but not irradiated. No negative effects of the irradiation on body weight, general state and skin of mice were noticed. Mice were tested several days after the single irradiation sessions. The cognitive task was based on mouse motivation to avoid the frightening brightly lit part of the box, in which it was placed initially, as there was the escape route - the underpass into the dark part of the box. The task required from an animal to find the covered underpass into the safe dark compartment of experimental box from the brightly lit uncomfortable area (puzzle box test). This task required that an animal understands the Piajetian «object permanence» rule. The reaction of mice to novel food in new environment had been tested too. Brains of experimental animals were investigated for the level of adult neurogenesis and for gene expression. In contrast to parental strain the hybrid

irradiated mice were significantly less successful in those task stages when the underpass was masked by wood shavings. At the same time they demonstrated the significantly more correct solutions when the underpass was blocked by a plastic-carton plug (more difficult for at animal). This enhancement was not found in mice of parental strains. Thus the single 4Gy irradiation induced the increase in logic task solution success (the reaction being performed more quickly as well) during the more difficult test stages. The «hybrid vigor», found in this study, underlines the importance of animal genotype as the important variable in irradiation experiments. The data as a whole show the importance to perform the repetitive irradiations in order to study the plausible changes in cognitive abilities, as the enhancement after the single dose looks as unusual. The adult neurogenesis (in two forebrain proliferative zones – in dentate and periventricular areas) was decreased as the result of the irradiations while the TNF gene expression (preliminary data) was 3 times more intense in 2 months after the irradiation. c-Fos immunoreactivity was decreased and the number of GAD67 positive cells – increased after the single 4Gy proton irradiation. Experiments were in accordance with the EC Declaration 2010.

Supported by OFI Program, grant N17-29-01001 and State program AAA-A16-116021660055-1.

HUMAN PAIN THRESHOLD IN HYPOMAGNETIC ENVIRONMENT

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The problem of assessing the characteristics of the pain syndrome is extremely important in the provision of medical care. It is known that the perception of pain is subjective and depends on various factors. During the planned manned interplanetary flights, including to the Moon, a person will be in a hypomagnetic environment. The effects of this influence on the human body, including on pain sensitivity, are currently practically not studied.

Purpose. Assessment of the impact of hypomagnetic environment on the humans' pain threshold.

Methods. The subjects of this study were men (N = 8) aged 27 to 38 years, who took part in experimental studies with an 8-hour exposure to a hypomagnetic environment. Two methods were used to assess the state of the PST (pain sensitivity threshold): tensoalgometry (mechanical impact) and thermoalgometry (thermal impact). Saliva samples were also collected to determine cortisol levels. To identify the relationship of pain sensitivity thresholds with circadian rhythms, as well as functional asymmetry of the body PST was measured several times a day, on symmetrical parts of the body.

Results. The data obtained do not allow us to assert a significant effect of 8-hour exposure to GMC (hypomagnetic conditions) on PST ($p > 0.05$), which, however, may be due to insufficient exposure to GMC and/or insufficient sample size. The data obtained indicate that there is no significant effect of circadian rhythms, as well as the daily dynamics of cortisol levels on PST ($p > 0.05$), both in the Placebo group and under hypomagnetic conditions. The available results confirm the absence of significant effect of the functional asymmetry of the body on PST ($p > 0.05$), both under the effects of Placebo and GMS. Also, the results indicate the comparability of the PST indicators obtained by the tensoalgometry method, both with a single measurement, and with the use of an average value, based on the results of a three-time measurement at intervals of 30 seconds (recommended in some algometry methods).

Obtained results do not allow us to assert a significant effect of 8-hour exposure to GMS on the level of cortisol ($p > 0.05$). The level of cortisol in saliva was expected to differ significantly during the measurement in the morning, at 10.05–10.25, and in the evening, at 20.30–20.50 ($p < 0.05$). Saliva cortisol levels were expected to correlate with height, weight, and body mass index ($p < 0.05$). At the same time, weight was determined as an independent predictor associated with cortisol levels ($p < 0.05$). Absence of correlation (unlike all other points) between these parameters and the cortisol level after exposure to GMS ($p > 0.05$), suggests the presence of an additional influence factor, which may be GMS.

Conclusion. Thus, it can be assumed that the 8-hour hypomagnetic exposure does not significantly affect the threshold of pain sensitivity in humans. In addition, the hypothesis about the influence of functional asymmetry of the body on the studied indicator was not confirmed. At the same time, no diurnal fluctuations of cortisol were detected under hypomagnetic conditions, which indicates the feasibility of continuing research in this direction.

HUMAN PAIN THRESHOLD IN SPACE FLIGHT

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During a long stay in microgravity and confinement, astronauts may experience changes in the state of sensory systems and the development of various pathological processes including injuries and diseases, which are usually associated with a feeling of pain. In this regard, an accurate interpretation of the dynamics of pain perception, assessment of its characteristics

and conditions leading to changes in the sensitivity to the pain factor in space flight conditions is extremely important in the provision of medical care.

Methods. The study was conducted as a part of the space experiment «Algometry». The value of pain threshold to mechanical (tensoalgometry) and thermal (thermoalgometry) effects was determined using a specialized device «Algometer». This work includes the results of the study of pain threshold of 10 cosmonauts. The study was carried in the pre-flight period, three times during the flight and twice after the cosmonauts landing.

Results. According to ANOVA Friedman comparing the pre-flight, early-flight, mid-flight, and end-flight tensoalgometry parameters, as well as on days 2–7 and 5–12 after the flight statistically significant differences were found ($p = 0.017$). A subsequent pairwise comparison using the Wilcoxon test revealed that the baseline parameters of the tensoalgometry were significantly lower than those in flight and after it.

According to ANOVA Friedman comparing the pre-flight, in-flight, and post-flight thermoalgometry parameters statistically significant differences were found as well ($p = 0,029$).

A subsequent pairwise comparison using the Wilcoxon test revealed that the pre-flight parameters of the thermoalgometry were significantly lower than those in the end-flight.

Conclusion. The obtained results indicate a tendency to increase the threshold of pain sensitivity in space flight. After the cosmonauts return to Earth, the pain threshold remains elevated for some time.

FIRST RESULTS OF THE HUMAN INNATE IMMUNITY RESEARCH DURING THE 21-DAY «DRY» IMMERSION WITH AN ARTIFICIAL GRAVITY USED AS A COUNTERMEASURE

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During the experiment with 21-day «dry» immersion (DI) with the use of artificial gravity as a countermeasure, the state of innate immunity of the human body was assessed.

As a result of the experimental influence, it was shown that the dynamics of changes in the relative and absolute content of monocytes expressing TLRs with intracellular and surface localization was characterized by rather high individual variability, however, for all studied subpopulations of monocytes expressing TLRs, it was shown that a significant changes in the number of cells, as well as in their expression of the corresponding markers, and the changes for the vast majority of receptors are noted towards a decrease in the studied parameters.

In the study, no pronounced change in the absolute content of monocytes was observed, while the relative content of peripheral blood monocytes also tended to decrease, except for 7 days, when their relative number increased compared to the background value.

The level of all cytokines - IL-1-beta, IL-6, IL-8, IL-10, IL-12, TNF-alpha, IFN-gamma, IFN-alpha, GM-CSF in blood serum, changed throughout the experiment, Moreover, all measured cytokines are characterized by a decrease two days before the start of exposure. In addition, it should be noted a tendency towards a decrease in the level of almost all cytokines under conditions of a 21-day stay in SI conditions using short-radius centrifuge as a means of prophylaxis, except for IL-6 and IL-8, the concentration of which during the experiment increased in comparison with the seventh day before DI.

The spontaneous synthesis of cytokines by cell cultures throughout the experiment showed a tendency to increase for almost all of the studied cytokines, except for Il-8, the level of which decreased compared to the background value. The data obtained in the experiment with DI using artificial gravity differ from that obtained in the previous experiment, in which in cell cultures spontaneous synthesis tended to decrease during the experimental exposure.

When cell cultures of monocytes were stimulated with the corresponding ligands of TLRs, the induced synthesis of cytokines had a pronounced individual character throughout the experiment, which does not currently allow any unambiguous conclusion regarding the emerging trends.

In general, it should be noted that the preliminary data obtained as a result of the implementation of this project confirm the hypothesis that, 2 days before the start of the experiment, the observed changes are caused by a psychological factor. In addition, a cautious assumption can be made that the use of artificial gravity, created be short radius centrifuge under DI conditions, has an activating effect on the synthesis of cytokines by monocytes in stimulated and non-stimulated cell cultures.

The work was supported by RSF grant №18-75-10086.

INFLUENCE OF REDUCED MAGNETIC FIELD ON HUMAN CENTRAL HEMODYNAMICS

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The influence of hypomagnetic conditions on the human body is still a poorly understood issue. At the stage of preparation for future manned space flights beyond low-Earth orbit, there is an urgent need to study changes in the psychophysiological status of a person under short-term exposure to a low Earth magnetic field.

In the Institute of Biomedical Problems of the Russian Academy of Sciences (IBMP RAS) studies were carried out with the participation of 8 healthy male volunteers (average age 33.3 ± 1.3 years). The purpose of the experiment was to study the influence of the modelled factor of the hypomagnetic environment (reduction of magnetic field about 1000 times) on cognitive, operator functions, the auditory analyzer, pain sensitivity indicators and the cardio-respiratory system of the human body under conditions of 8-hour exposure in a hypomagnetic environment. The study was conducted in 3 stages – a training session (to familiarize with the experimental conditions), placebo and exposure (randomized double blind).

When adapting the organism to any changing environmental conditions, regulatory mechanisms change parameters of the cardiovascular system. With the help of «Mobilograph» device, which is used by cosmonauts on the International Space Station, data on central hemodynamic parameters under hypomagnetic conditions were obtained for the first time.

Hemodynamic analysis plays a crucial role in assessing the risk of cardiovascular disease, it provides an opportunity to assess the «age» of the arteries and those changes that will be necessary to make a decision on the appointment of additional studies or treatment.

Data on heart rate, central aortic pressure, stroke volume, peripheral vascular resistance, and pulse wave propagation velocity were obtained. As a result of comparing the data of the two tests, it was suggested that the decrease in the magnetic field (of the indicated duration) does not affect the central hemodynamics in a reliable value. It is concluded that studies should be continued with an increased duration of exposure and the number of subjects for a better understanding of the mechanisms of adaptation of the cardiovascular system to conditions of hypomagnetic exposure.

The research was carried out within the framework of the RAS base topic 64.1 for 2013-2023 years.

GAS EXCHANGE AND VENTILATION IN HEALTHY HUMANS DURING 8-H HYPOMAGNETIC EXPOSURE

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The detailed studies of physiological effects of hypomagnetic fields on human beings is extremely needed for planning of the long-term interplanetary flights in nearest future. There are no sufficient data of ventilation and gas exchange in biological objects under low magnetic exposure (Binhi, 2017). Fu et al. (2016) had shown that hypomagnetic exposure reduces energy production and mitochondrial activity of primary mouse skeletal muscle cells. Since these observed changes may be accompanied with the resting energy expenditure the aim of our study was to estimate the oxygen consumption (VO_2) and carbon dioxide production (VCO_2) and its ratio via indirect calorimetry in healthy humans under hypomagnetic field exposure. Eight healthy male volunteers participated in double-blinded randomized study (hypomagnetic field and control sessions in separated days). The facility «ARFA» (IBMP) had been used for modeling of magnetic environment for both experimental days. Lung volumes and flows were measured before and after exposure by spirometry in the laboratory room, whereas ventilation and exhaled gas monitoring was provided on 8 h sustained hypomagnetic exposure/control in «ARFA» facility. The equipment Oxycon Mobile (Jaeger, Germany) was used for all measurements. Spirometric parameters as to be expected had no changes during experiment in all subjects. Breathing rate and minute ventilation has no changes during experimental exposure as well as between the sessions. The indirect calorimetry was carry out 5 hours after small meal (<300 kcal) before the end of hypomagnetic/control impact. The results had been shown that $R = VCO_2/VO_2$ was significant lower in hypomagnetic field compared control (0.83 ± 0.03 vs 0.86 ± 0.03 respectively, $p < 0.03$, paired Wilcoxon test) on 8 h exposure, it may possibly indicate declined oxidation processes at mitochondrial level. These obtained pilot data need to provide further studies.

The research was supported by RAS program for IBMP fundamental studies (N 64.1).

TRANSCRIPTOMIC SIGNATURES AND UPSTREAM REGULATION IN HUMAN SKELETAL MUSCLE INDUCED BY INACTIVITY AND AEROBIC EXERCISE: A META-ANALYSIS

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Inactivity is associated with the development of numerous disorders. Regular aerobic exercise is broadly used as a key intervention to prevent and treat these pathological conditions. In our meta-analysis we aimed to identify and compare i) the transcriptomic signatures related to in-activity, regular and acute aerobic exercise in human skeletal muscle, and ii) the biological effects and transcription factors associated with these transcriptomic changes. A standardized workflow with robust cut-off criteria was used to analyse 27 transcriptomic datasets for the vastus lateralis muscle of healthy humans subjected to inactivity, regular and acute aerobic exercise. We evaluated a role of transcriptional regulation in the phenotypic changes described in the literature. The responses to chronic interventions (inactivity and regular training) partially correspond to the phenotypic effects. While acute exercise induces changes that are mainly related to the regulation of gene expression, including a strong enrichment of several transcription factors (most of which are related to the ATF/CREB/AP-1 superfamily), and a massive increase in the expression levels of genes encoding transcription factors and co-activators. Overall, the adaptation strategies of skeletal muscle to decreased and increased levels of physical activity differ in direction and demonstrate qualitative differences that are closely associated with the activation of different sets of transcription factors.

This research was funded by the Russian Foundation for Basic Research (RFBR), grant No. 17-00-00308K (17-00-00242) and No. 19-315-90135.

THE METHOD FOR DIRECT MASS SPECTROMETRIC ANALYSIS OF BIOLOGICAL SAMPLES USING POROUS SAMPLERS

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The implementation of multi-omics techniques in gravitational physiology has created the need to address many technical challenges related to the development of methods for sampling, transporting, and analysis of various biological specimens. Thus, it is required to monitor the cosmonaut's wellness before, during, and after the flight. To perform the sampling procedure during the space flight, it has to be simple, and samplers have to be compact and lightweight. Here we present a method for rapid multi-omics investigation of biological samples using polypropylene bulk porous samplers. The use of porous samplers makes it easy to collect samples from the surface of the skin, mucous membranes, and biological fluids. The collected samples do not require special storage conditions (like refrigeration) in a micro-g environment or during transportation from the orbit. The analysis of biomaterial applied to the sampler is performed using direct mass spectrometry methods, similar to the dried blood spot technique that is already used in clinical practice. However, bulk porous samplers allow expanding the range of analytes ionization conditions, which increases the stability and reliability of the ionization process, which expands the variety of analyzed molecules. We demonstrate this technology in application to detect proteins and monitor the presence of toxins and their metabolites on the skin surface and in blood after intake. The proposed method can be used to study compounds of various classes, including proteins, lipids, and metabolites, to systematically monitor the status of people in extreme conditions.

THE RELEVANCE OF ANTICIPATION TO THE SEARCHES FOR ALIEN LIFE IN ASTROBIOLOGY

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The scientific searches for alien life in astrobiology focus on biosignatures and, more recently, also on technosignatures. According to Des Marais and Jahnke (2019), a biosignature is an object, substance, and/or pattern created by a biological source, the value of which is also partially determined by the improbability of non-biological processes producing it. Tarter (2007) has defined the concept of technosignatures as evidence of some technology that modifies its environment in ways that are detectable, in particular, evidence of equivalents of some 21st century terrestrial technologies. As the search for

biosignatures requires a working definition of life's fundamental characteristics that will also take into account instances of unknown life that could be very different from the terrestrial one, it becomes evident that uncertainty is a critical factor in the process of identifying and interpreting biosignatures. In parallel, the search for technosignatures is also thought to be able to contribute to the search for alien life by permitting the inference of «the existence, at least at some time, of intelligent technologists». Judging by the aforementioned conceptualizations, it seems that the discipline of Anticipation that is strongly related to uncertainty may be relevant to the search for alien life and may offer insights to proactively facilitate the further development of this scientific field. According to Poli (2017), Anticipation Science encompasses natural, formal, and social systems that intentionally or unintentionally use ideas of a future to act in the present, with a broad focus on humans, institutions, and human-designed systems. As the third level of Futures Studies after forecasting and foresight, by definition, Anticipation includes two mandatory components: a forward-looking attitude, and the use of this attitude's result for action in the present. Both the search for biosignatures and the search for technosignatures seem indeed to be forward-looking endeavors that use definitional constructs of life and technology beyond Earth, the discoveries of which lie in the future, in order to guide the necessary actions for these discoveries in the present. Therefore, by highlighting the major ways in which

Anticipation is relevant to the search for alien life in astrobiology, a case is made for the potential usefulness of approaches based on the concepts of Anticipation-for-the-Future and Anticipation-for-Emergence as complementary to other interdisciplinary activities, such as education and outreach, that share the common goal of strengthening this scientific endeavor. Perceiving the search for alien life through the lens of Anticipation can provide a fertile ground for novel theoretical and empirical investigations of multiple individual and collective facets of the human factor pertaining to the discovery of alien life and its implications, thereby catalyzing the preparation for and the management of the bespoke discovery.

OPERATION OF THE RUSSIAN «ELECTRON-VM» OXYGEN GENERATION SYSTEM ABOARD THE INTERNATIONAL SPACE STATION

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The Russian oxygen generation system (OGS) «Electron-VM» operates at the International Space Station (ISS) since 2000. The OGS generates oxygen for the crew consumption and consists of a processing unit (PU), a signal-command connection unit (SCCU) and the connecting cables set (CCS). PU generates oxygen and hydrogen by water electrolysis on an alkaline electrolyte (25 % by mass KOH solution) in a flow-through electrolyzer, which is followed by the gas-liquid mixture separation in static separators and catalytic oxygen purification. The electrolysis current is 10–64 A (current density is 0.03-0.21 A/cm^2), the oxygen production is 25–160 normal l/h.

As of 01.01.2021, the «Electron-VM» OGS on the ISS 4694 days operated (not including downtime), oxygen produced 11307 kg, water used 12972 kg (12720 kg used for electrolysis and 252 kg of removed of water vapor). Maintenance time for the OGS ≈5 man-hours per 100 kg oxygen. OGS components were replaced several times for reasons such: PU - fatal failure, SCCU and CCS – long-term work beyond lifetime (without failure). Since 2000, in the OGS (including currently operational) were used: PU (mass 160 kg) 8 pcs., SCCU (mass 3.5 kg) 6 pcs. (including 1 pc. on-board reserve), CCS (mass 1 kg) 2 pcs., additional equipment (including onboard spares) 79 kg. In the systems, that support the operation of the OGS, the following was used: a nitrogen supply unit (nitrogen pressurization of the PU, mass 15 kg) 10 pcs., a multifiltration unit (feed water purification for the PU operation, mass 18 kg) 33 pcs., electrolyzer power supply equipment 74 kg, air revitalization and monitoring system equipment 25 kg.

The main OGS advantages based on the operation results:

– real electrolyzer voltage (12 cell stack) 18.90-22.15 V (depends on the oxygen production);

– energy consumption: for electrolysis average is 8.2 ± 0.1 Watt-hour per normal liter of oxygen and less than 10 Watt for all equipment (SCCU, pumps, valves, sensors);

– feed water for the PU operation allows conductivity (determines the trace contamination total content) up to 180 μS/cm and the bacterial contamination up to 100 thousand microbial bodies per 1 ml;

– parameters stability during long-term operation;

– multiple (hundreds of times) switching on and off and pauses in operation from several minutes to two months without any additional maintenance;

– stability to off-normal situations (ONS);

OGS «Electron-VM» development since 2000:

– PU continuous upgrade based on operating experience;

– PU and its components are produced at «NIIchimmash»;

– operation support system;

– systematic approach to the OGS;

– the PU operating time onboard ISS is 1265 days before failure at the previous unit (in 2006-2011) and 1979 days without failure at the current one (since 2011);

– minimization of ONS number on board;

– created and applied a set of additional equipment for the PU (to overcome ONS, extend the operation life and improve safety).

Further OGS development:

– reach 7 years of PU operating time;

– OGS technical state forecast.

INFLUENCE OF GRAVITY ON ORGANIZATION OF EYE MOVEMENTS AND VISUAL PERCEPTION

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Research of Dr. L.N. Kornilova and her colleagues from Institute of Biomedical Problems of Russian Academy of Sciences showed that functioning of vestibular and body position systems are connected with visual perception. It is well known that absence of gravity influences visual perception. Visual illusions and nystagmus appear in cosmonauts during first days of their space flight. That was described in works of Dr. L.N. Kornilova and other authors.

It is well known from the works of Hubel D.H. and Wiesel T.N. (2005) about the activity of sensory areas. The research of retinal receptive fields and visual centers in immobilized animals showed that hyper complex cells of receptive fields become active by movement of the line, which is perpendicular to the movement direction in the receptive fields zone. And these receptive fields are activated by the line moving in one direction only (by black line on white field or white line of black field). The activity of motor area is known from works of Dr. A.R. Shahnovich (1974), stipulating that tremor emerges during drift and is a result of high-frequency discharges in nerves which control eye movement muscles. These impulses bring oculomotor muscles into the state of tetanus. And this exact state leads to emergence of drift with tremor.

Our personal research of eye movements and binocular vision mechanisms and literature study led us to the idea that organization of eye binocular and monocular micro movements is under influence of gravity that is necessary for codification of visual information from the retinal receptive fields as well as decodification and processing of this information in visual centers.

It is obvious from our research that drift with tremor is performed in direction of gravitational field in most experiments. Observation of the eye movement trajectory makes it possible to conclude that tremor is near perpendicular to drift. Consequently, it is drift with tremor, which exactly allows to activate on-off and off-on retinal receptive fields and to code visual information. These eye movements are an equivalent of the line moving along retinal receptive field. Our idea gives explanation why nystagmus emerges in cosmonauts. For codification and reading of visual information in conditions of the gravity absence it is necessary to increase the amount of saccades and micro saccades alternating them with micro drift with tremor. But visual illusions emerge not only due to the vestibular system dysfunction but to dysfunction of propriocenters of oculomotor muscles during gravity absence. All this leads to dysfunction of eye movement coordination and as a consequence to visual illusions.

Conclusion: We suppose that gravity influences the eye movement organization that in its turn influences visual perception. We suppose that trainings with virtual visual images in physiological diplopia (Rabichev I.E., Kotov A.V. 2019) could accelerate adaptation of visual system in gravity conditions.

AN APPROACH TO DEFINE REQUIREMENTS AND EVALUATION PHILOSPOHY FOR CREW COMFORT IN SHORT DURATION HUMAN SPACEFLIGHT MISSION

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It has been more than six decades since Humans travelled into space. Human space flight is guided by a set of requirements with constraints imposed by human physiology. These requirements are taken into consideration right from the design phase and are rigorously implemented during reali-zation and operation of spacecraft. With all our expertise and global pedigree in Human space flight, it is time to think over and above human requirements with due importance to crew comfort. In this paper, the authors have made an effort to quantitatively define human comfort levels. These levels are above and inclusive of basic human physiological requirements.

Presently professional astronauts are selected among the fittest of the candidate population and undergo rigorous training and acclimatisation regime to overcome these challenges. Usually, the training is categorised into regimes like basic

flight training, advance training and mission-specific training which lasts for years. Unlike the rigorous training received by professional astronauts, Tourist-astronauts or Tuoristonauts who enrol for space tourism flight will undergo only a basic level of train-ing before their space flight. The expected mission duration for tourist astronauts is going to be shorter ranging from 1–3 days, thus onus lies on the spacecraft designers to provide the Tourist-astronauts with a pleasurable experience of space travel.

Human factors engineering is a multi disciplinary field involving Science, Engineering and Humani-ties. It basically deals with interaction between humans and other elements of a system. It is a field which strives to srike a balance between optimized system performance and Human well-being. These Human factors play a critical role in quantification of crew comfort.

Standards practice and protocols exist for defining and adressing crew comfort requirements for long duration missions and bigger habitats volumes. To provide crew comfort for a short duration missions and specifically for a relatively small habitat is a greater challenges for system designers.

This paper highlights the human factors critical to a short duration mission for a smaller habitat volume and the challenges associated with them. The challenges extends from designing the human habitat, crew tasks to selection of suitable human centric products. This paper also discuss on the quantification of the crew comfort for such mission using tools such as standard questionnaires, ground based simulation, human trials etc..

The philosophy proposed for evaluation of crew comforts levels will involve trials such as environ-mental chambers, high-g and low-g simulations, hypobaric test chambers for human centric produts such as flight suits, garment etc. disorientation/ dynamic simulations for crew interfaces and controls, isolations trials & wetbed/dry supine immersion studies for psychological and palatability of space food, neutral byouyancy studies for development of protocols. The test requirement will be cutomised for crew comfoart evaluation with respect to targeted human factor for each tests. Crew feedback obtained will be used for defining a close loop approach for crew comfort levels.

The methodlogy discussed in this paper is aimed towards developing a novel scale of reference for defining crew comfort for shrot term mission and small habitable volumes, which is currently una-viliable. Through this study the aurthors have addressed the Crew comfort requirements for a short duration mission. The outcome of the study will be evolving a scale of reference for defining human comfort levels.

INACTIVITY AND UNLOADING AS DETERMINANTS OF MUSCLE IMPAIRMENT IN MICROGRAVITY

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Human body has been designed by millions of years of evolution to live and move in an environment characterized by a significant gravitational acceleration of 9.8 m/s^2. Several important adaptive changes involving many organs and systems accompany the transition to environments where gravity is virtually absent as in the orbital International Space Station, where gravitational acceleration is compensated by centrifugal acceleration, or to future Lunar or Martian environments where gravitational acceleration is lower than on the Earth.

Among the organs responding to the change in gravitational acceleration, skeletal muscles adapt to the new conditions with a rapid loss of mass (atrophy) and an even more pronounced loss of contractile performance.

While atrophy is the result of a new balance between protein synthesis and degradation, several factors from altered neuro-muscle connection, to sarcoplasmic reticulum impairment and myofibrillar motor impairment are considered responsible for the loss of contractile force.

The intracellular signaling cascades linking the reduced gravity to molecular and functional alterations are still the object of investigation as several aspects remain debated. A first interesting question deals with the respective roles of reduced mechanical loading and decreased electrical activity and the identification the molecular sensors able to trigger the intracellular signaling chains. A second open field of investigation is which signaling pathways and molecules are involved. Finally, the reasons of discrepancy between functional and structural impairment are still debated.

Alterations of the NMJ, signs of partial denervation with appearance of NCAM positive fibers, changes in fiber type with a slow-to-fast transition, alterations of the calcineurin-NFAT signaling point to a major role of the decrease of neural stimulation on muscle fibers. Such decrease can be due to the reduced cortical discharge as less motoneuron activity is required for movements or to the loss of reflex and automatic activity finalized to postural stability. In parallel, an unbalance between the Akt-mTOR pathway supporting ribosomal protein synthesis and the degradation pathway centered on proteasome and autophagy support the relevance of the reduced mechanical load.

In this presentation, the open questions will be discussed comparing results of studies on cosmonauts where the effects of microgravity are partially modified and mitigated by necessary countermeasures and studies on volunteers exposed to well defined experimental conditions such as bed rest, unilateral limb suspension and immobilization.

POSSIBILITIES FOR TREATING SENSORIMOTOR DISTURBANCES IN ASTRONAUTS AND COSMONAUTS AFTER LONG-DURATION SPACE FLIGHTS

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A joint NASA and Institute of Biomedical Problems (IBMP) study, designated as the *Field Test*, was designed to investigate the immediate postflight effects of long-duration spaceflight on the sensorimotor, vestibular, and proprioceptive systems, and to track these changes using tests of sensorimotor and functional behavior associated with everyday living. Results of the Field Test have shown that the existing inflight countermeasures, which rely heavily on strength and endurance, are not adequate to prepare the crewmembers for postflight recovery without the assistance of extensive landing support personnel. New and specific preflight, as well as potential inflight countermeasures must be designed and tested to enable crewmembers to function autonomously immediately after they land. We will explore some nontraditional and untried strategies designed to prepare and assist crewmembers to safely egress from their spacecraft after landing in water.

The current landing vehicle, the Russian Soyuz capsule, lands on Earth and it not subjected to wave motion, and the crew are assisted during egress by a significantly large landing party who carry the crewmembers from the space craft into the medical tent. Our body movements on Earth are highly ordered due to contemporaneous and sequential patterns of sensory messages that occur as a consequence of voluntary movement. This orderly pattern is obtained by the sensitivity and dynamics of the sensory organs themselves. We consciously make small corrections to our movements to correct our posture but these corrections are typically so automatic that we are not aware we are making them until a small error in movement is actually perceived and corrected.

During water landing, on the other hand, the environment will be unstable for several hours, and the crewmembers will very likely have motion sickness and spatial disorientation caused by the landing. Without assistance, egress from the landing craft will be very difficult. Use of orientation devices (artificial horizon similar to a Malcom Horizon, carefully controlled and titrated head movements in all cardinal planes, vibro-tactile feedback) within the capsule during re-entry could be beneficial and help mitigate disorientation, dizziness, vertigo, loss of equilibrium and oscillopsia. Preflight inflight and immediately postflight and be employed using velocities of variable magnitude should be explored as a countermeasure. For sea recovery training in different sea conditions will be mandatory and will help the astronauts to adapt their responses.

THE MICROBIOME OF THE INTERNATIONAL SPACE STATION (ISS)

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The International Space Station (ISS) is a unique, completely confined habitat for the human crew and co-inhabiting microorganisms. In the experiment EXTREMOPHILES we investigated the microbial bioburden and biodiversity from three surface and air sampling events aboard the ISS during increments 51 and 52 (2017) with respect to: i) microbial sources, diversity and distribution within the ISS, ii) functional capacity of microbiome and microbial isolates, iii) extremotolerance and antibiotics-resistance (compared to ground controls), and iv) microbial behavior towards ISS-relevant materials such as biofilm formation, or potential for degradation.

Wipe samples were analysed by amplicon and metagenomics sequencing, cultivation, comparative physiological studies, antibiotic resistance tests, genome analysis of isolates and co-incubation experiments with ISS-relevant materials.

The major findings were: i) the ISS microbiome profile is highly similar to ground-based confined indoor environments, ii) the ISS microbiome is subject to fluctuations and indicative for the location, although a core microbiome was present over time and independent from location, iii) the ISS selects for microorganisms adapted to the extreme environment, but does not necessarily induce genomic and physiological changes which might be relevant for human health, iv) cleanrooms and cargo seems to be a minor source of microbial contamination aboard, and v) microorganisms can attach to and grow on ISS-relevant

materials. Biofilm formation might be a threat for spacecraft materials with the potential to induce instrument malfunctioning with consequences for mission success.

We conclude that our data do not raise direct reason for concern with respect to crew health, but indicate a potential threat towards biofilm formation and material integrity in moist areas.

GAUSS PRECURSOR MISSION FOR MARS EXPLORATION

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The era of human interplanetary voyages in the Solar System is drawing near. New space technologies, combined with a growing number of available launchers and novel low-energy interplanetary trajectories allow costs and time optimizations, therefore reducing the timespan between interplanetary missions and increasing launch opportunities towards Mars.

GAUSS has been developing microsatellites since the 90s, when it was a laboratory of the School of Aerospace Engineering of Rome, before becoming a private company, GAUSS Srl, in 2013. The first microsatellite by GAUSS, named UNISAT, was launched in 2000 and in 2013 UNISAT-5 was the first platform to accomplish in-orbit-release of third-party satellites, with UNISAT-6 following in less than one year.

UNISAT-7, the latest addition to the UNISAT series, is a 32kg microsatellite ready to be launched in Q1 2021. UNISAT-7 is a complex and flexible platform entirely designed and manufactured by GAUSS, based on the experience gained in the past missions, and includes an optical payload, an ion-thruster and a three-axis attitude control system.

Recently GAUSS has been actively investigating interplanetary missions compatible with microsatellites of the UNISAT series, developing novel techniques for mission design. In fact, these missions can take advantage of low-energy trajectories existing in multi-body environment, such as the Sun-Earth-Moon and the Sun-Mars systems, leading to dramatic savings in the total propellant required to perform the orbit transfer and plane change maneuvers.

A robotic precursor mission is proposed in this work, aiming at collecting data on the cosmic ray environment surrounding Mars. In fact, solar energetic particles and Galactic Cosmic Rays (GCRs), composed primarily of protons and Alpha particles, are usually deviated or converted by terrestrial magnetosphere, but on missions extending through the Solar system, this particle flux shall be taken into account to calculate the Equivalent Radiation Dose expected for manned personnel. It is worth noting that a cosmonaut on a mission to Mars could receive radiation doses up to 200 times higher than on Earth.

The space probe deputed for the mission is a 70 kg microsatellite, which integrates several electro-optical sensors, as well as radiation and particle detectors, to provide meaningful data for next manned missions to the red Planet and contribute to a risk model for such missions. Due to the thin atmosphere of Mars, the radiation measured at low altitude is comparable to that measured on its surface. Furthermore, previous missions indicate that the cosmic radiation changes significantly with the latitude and longitude. In order to perform a detailed mapping of the cosmic ray environment in the surrounding of Mars, the probe will be injected into a Martian orbit whose apogee approaches the Sun-Mars equilibrium point L1. Such orbit shows chaotic behavior, then its orbit parameters can be modified by small maneuvers in the neighborhood of L1, adjusting the orbit plane and the orbit pericenter burning a small amount of propellant compatible with a microsatellite mission.

Knowledge of the radiation environment around Mars is critical for future manned missions, to develop an optimized transport vehicle for interplanetary missions passing through these zones.

HUMAN CAPABILITIES ASSESSMENTS FOR AUTONOMOUS MISSIONS: A MULTI-TEAM RESEARCH EFFORT TO REDUCE RISK IN THE HUMAN-SYSTEM INTEGRATION ARCHITECTURE FOR FUTURE DEEP-SPACE MISSIONS

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In future exploration missions beyond low earth-orbit, crew will have to execute complex operations and respond to off-nominal events, without real-time support from Mission Control. It is anticipated that increased reliance on automated systems, including human-centric vehicle and information architecture, will need to be designed to support the crew; increased risk to performance, health, and safety may occur if these are not implemented appropriately. The Human Factors and Behavioral Performance Element (HFBP) in the NASA Human Research Program supports research to characterize and mitigate such human health and performance risks, including the Risk of Adverse Outcome Due to Inadequate Human Systems Integration Architecture (HSIA).

The HSIA risk addresses the integration of onboard capability and the crew roles and responsibilities necessary to enable the crew to respond effectively and efficiently in the increasingly autonomous mission operations environment. In 2017, HFBP

released the «Human Capabilities Assessments for Autonomous Missions» (HCAAM) research topic to address HSIA related questions. HCAAM is a major NASA research effort that has assembled a multidisciplinary team from seven institutions to work closely with design and engineering efforts on research towards developing and refining human performance standards, guidelines and automation tools. The scientific focus is on quantitative assessment of human capabilities relevant to future deep-space missions during which earth/spacecraft communication is so delayed and intermittent that the crew must be able to function autonomously.

The integrated strategy of the HCAAM project characterizes human capabilities and limitations related to potential performance decrements during long duration exploration mission spaceflight as relevant to both routine and complex task performance; defines system characteristics that reduce the likelihood or impact of potential decrements in human performance capabilities; performs integrated assessment of intelligent system responses within the context of an operational environment with relevant NASA tools, systems, and data structures in order to determine positive or negative interactions and validate recommended approaches; and proposes specific updates to existing standards and guidelines for inclusion in NASA handbooks for the design of future spacecraft intelligent systems that provide crew performance assessment/feedback, and to also serve as decision-support aids for the onboard crew (i.e., NASA-STD-3001, and NASA/SP-Human Integration Design Handbook (HIDH)).

The scientific research vectors being addressed by the seven HCAAM teams include:

– crew task performance (accuracy, efficiency) (crew + automation);
– crew performance (accuracy, efficiency);
– crew Situation Awareness;
– procedure design and multi-modal enhancement;
– concurrent tasking (mixed manual + some level of autonomy);
– task handover;
– crew self-planning and time-lining;
– task design;
– trust in automation, real-time calibration;
– human multi-sensory feedback and guidance;
– human trust in on-board software-based intelligent assistants;
– virtual assistants.

The presentation will highlight plans and progress made in each of these research areas as well as the methods by which surrogate astronaut crews in the NASA JSC HERA spaceflight analog facility will function as human test subjects for all of the HCAAM research projects.

STRENGTH-TO-WEIGHT INDEX AT READAPTATION TO EARTH CONDITIONS AFTER REPEATED SPACE FLIGHTS

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Relevance. Occupational tasks performance success during space flight (SF) and in the acute period of readaptation after its completion depends on the state of health, the physical performance level. Physical training during SF makes it possible to maintain the strength of the cosmonauts' leg muscles at a sufficient level for solving simple tasks like walking immediately after landing.

Currently, tests and criteria for successful occupational tasks prediction are being actively developed. The strength-to-weight indicator is used in assessing the post-flight state of the neuromuscular system of astronauts (Dos'Santos T, et. all., 2017; Ryder JW, et. all., 2013; 2019; Kirk L. English, et. all. 2020). The question arises about the effects repeated 0-g exposure on the cosmonauts' adaptation and readaptation to the conditions of the Earth. In addition, it is necessary to determine the modes of physical training performed during SF to maintain muscle strength level sufficient for occupational tasks performance.

The aim of the study is to determine the minimum threshold strength value for the leg muscles, which is necessary for the successful fulfillment of professional tasks in the acute period of readaptation to gravity.

Methods. A comparative analysis of the change in the body mass of 13 cosmonauts who performed repeated SFs on the ISS with duration of 156–187 days was carried out. The cosmonaut's body mass was estimated before SF and at the final stage of SF. The obtained data on the body weight of the cosmonauts and the results of isokinetic testing of the leg muscles were used to calculate strength-to-weight ratio (STW). The data of the same crew members were compared after two latest SFs. During SF, the cosmonauts performed strength training every other day as recommended by Russian specialists.

Results. A significant decrease in thigh extensor muscles STW was observed both after the first ($P = 0,001$), and after the second SF ($P = 0,03$). The decrease in strength after the first SF was more pronounced than after the second one ($P = 0,05$).

The leg extensor and flexor muscles STW decreased significantly only after the first SF: the losses were 16,7 ± 6,2 % (P = 0,02) and 15,5 ± 7,1 % (P = 0,03) respectively; after the second SF the changes did not reach statistical significance.

The criterion for assessing leg muscles STW was developed for "leg hatch-opening" task in an experiment with 70-day antiorthostatic hypokinesia. Based on this model experiment, it was shown that an astronaut must have a thigh muscle STW of at least 1,83 N·m/kg (Ryder JW, 2019; Kirk L. et al., 2020). The results of our research indicate that STW in the «extension in the knee joint» test after the first SF was 2,00 N·m/kg, after the second SF – 2,14 N·m/kg. That is, in both cases, exceeds STW threshold. Thus, the strength training performed by the cosmonauts every other day during SF, in accordance with the recommendations of Russian specialists, is sufficient to maintain the strength of the leg muscles at the required level to perform certain occupational tasks.

Conclusion. The decrease in STW is more pronounced after the first SF than after repeated SFs.

Supported by basic funding from RAS 63.1.

THE IMPACT OF DEEP SPACE RADIATION ON COGNITIVE PERFORMANCE: FROM BIOLOGICAL SEX TO BIOMARKERS TO COUNTERMEASURES

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Exposure to galactic cosmic radiation (GCR) is a major obstacle for deep space travel. Given the concern that GCR exposure induces changes that could affect cognitive performance either during and/or after a prolonged mission, the purpose of this work was to determine how space relevant doses of charged particle radiation affect synaptic functions. We hypothesized that space radiation, even at low doses, impairs synaptic functions with negative consequences for cognition. Further we hypothesized that these effects are mediated by inflammation in a sex dependent manner. First, we demonstrated that four months after a single exposure to oxygen ionizing radiation, a component of GCR, adult male mice report social memory deficits. We identified circulating levels of CD8 T cells to be predictive of the changes in social behaviors. For the first time we demonstrate that GCR-induced impairments in social behavior are directly linked to peripheral immune changes that could be used as a predictive biomarker. Second, we investigated how combined GCR impacts long-term behavioral and cellular responses in male and female mice. Single exposure to simulated GCR induces long-term cognitive and behavioral deficits only in the male cohorts. GCR exposed male animals had diminished social interaction, increased anxiety-like phenotype, impaired recognition memory and deficits in spatial learning. Remarkably, we found that the female cohorts did not display any cognitive or behavioral deficits after GCR exposure. Mechanistically, the maladaptive behavioral responses observed only in the male cohorts corresponded with microglia activation and synaptic loss in the hippocampus, a brain region involved in the cognitive domains reported here. Furthermore, we measured reductions in AMPA expressing synaptic terminals in the hippocampus. No changes in any of the molecular markers measured were observed in the females. Third, we demonstrated that temporary microglia depletion, one week after cosmic radiation, prevented the development of long-term memory deficits in male. Gene array profiling reveals that acute microglia depletion alters the late neuroinflammatory response to cosmic radiation. At the cellular level we find the repopulated microglia present a modified functional phenotype with reduced expression of scavenger receptors and lysosome membrane protein both known to be involved in microglia-synapses interaction. The lower phagocytic activity observed in the repopulated microglia is paralleled by improved synaptic protein expression. Our data provide mechanistic evidence for the role of microglia in the development of cognitive deficits after cosmic radiation exposure in male mice. We are currently investigating the effect of Simplified Mixed Field Standard Mixture exposure, the progress on this project will be discussed.

This study was supported by NASA grants NNX14AC94G and 80NSSC19K1581 to Rosi S.

PSYCHOLOGICAL SUPPORT BASED ON VIRTUAL REALITY IN SIMULATION EXPERIMENTS, ISOLATION AND SPACE FLIGHTS

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For people who are in isolation (hospital or quarantine conditions, highly autonomous professional activities, space flights, etc.), a number of negative psychoemotional manifestations associated with sensory «hunger» are characteristic. Psychological support for such persons mainly consists in the reconstruction of the natural sensory «influx» and in the restoration of the

image of their usual life. For this purpose, in cases where full-fledged psychological support with the direct participation of psychologists is difficult, it seems appropriate to use virtual reality complexes (VR), which provide replenishment of the usual visual range for «norma» life and promote active spending of personal free time. Application of VR technologies in space flights, especially in interplanetary flights, is promising. The specifics of interplanetary flights will be accompanied by a number of new psychogenic factors, many of which (the «break-off» phenomenon, erasure of the image of the Earth, lack of day and night changes, lack of personal space). Psychological support based on VR can serve as an effective counter-measure for those factors.

Currently, VR systems used as a method of psychological support are being tested in ground experiments that simulate the conditions of space flight. Thus, during the SIRIUS-19 isolation experiment, the positive effect of VR on the psychoemotional sphere of the crew members was shown.

In the 3-day «dry» immersion simulation experiment with the participation of 6 recepients, a program of psychological support based on VR was tested. This system was developed for subjects under conditions of acute hypokinesia. The selection of 3D materials was based on recipients' individual preferences. This materials included three-dimensional videos of nature, marine animals, diving. Research program included questionnaires, interviews, self-reports of the testers recorded on a digital camera before and after the VR session (followed by an objective analysis of facial expressions) and actigraphy (an objective method). Content analysis of the recepients' speech was also carried out. The following was established:

1. According to actigraphy data, the maximum of the motion vector during a VR session is lower than this maximum on average per day. (This is a phenomenon that could be called «subsiding».) This allows us to assume that during the psychological support session, the recepients have the maximum concentration of attention.

2. Percentage of parasitic words and speech errors from the total volume after the VR session also decreases.

3. According to a computerized facial expression analysis, after the VR session, there was a harmonization of emotions of recipients.

Studies in «dry» immersion have generally confirmed positive psychological effect of using psychological support with the use of VR.

The study was supported by the Ministry of Science and Higher Education of the Russian Federation under the agreement No. _075-1502020-919 from 16.11.2020 about the grant in the form of subsidy from the federal budget to provide government support for the creation and development of a worldclass research center "Pavlov Center for Integrative Physiology to Medicine, High-tech Healthcare and Stress Tolerance Technologies".

A VISION ON PSYCHOLOGICAL SUPPORT IN FUTURE INTERPLANETARY SPACEFLIGHTS

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Modern system of psychological support of the orbital flights can be regarded as an effective countermeasure against the negative impact of sensory deprivation, monotony and confinement, as well as deprivation of social contacts occurring during extended space mission. But some approaches and methods of psychological support that are used during orbital spaceflight (such as re-supplies, on-line private conference with psychologist, uplink of the current news, regular conferences with family members and notable persons) would be unavailable in missions to Mars and to other planets due to impossibility of their logistic support and delays in communication with Earth. Also the new risks related to the loss of home planet vision, described by Kanas and Manzey (2004) the «break-off phenomenon», as well as communication delay could significantly deteriorate crew morale, causing depression and breaking of social contacts (Gushin, Shved, Yusupova et al 2014).

The proposed concept of prospective psychological support in autonomous space flights is based on the assumption that it is necessary to artificially recreate the missing elements of mundane human environment, to re-establish broken «cultural roots». To succeed, such new tools as virtual reality (VR), simulation of natural light and biorhythm sensors, biological objects (greenhouses, aquariums, etc.), as well as robotic devices that emulate «live» communication, (voice and/or virtual assistants) can be used in addition to the standard measures of psychological support.

Virtual reality tools promote both relaxation, being an attention-grabbing form of leisure, and a way to immerse into the familiar image of the Earth, daily life and culture. In SIRIUS-19 isolation experiments, the beneficial effect of virtual reality on the psycho-emotional sphere was demonstrated for the most of the international mix-gender crew.

The general tasks of virtual reality complexes used for psychological support are:

1. Restoration of the image of habitual life and its qualia; restoration the effigy of the surrounding nature, «erased» from memory during isolation or space flight, including loss of the vision of the home planet.

2. VR as a specially composed organized form of leisure, psychological training and recreation (a counter-measure to monotony and fatigue).

3. Filling the deficit of personal space by creating its virtual analog as a countermeasure to the forced socialization on board of spaceship.

4. Filling the deficit of non-professional communication. This deficit can also be filled by using robotic devices and voice assistants. Robotic devices and voices assistants can be important not only to compensate the lack of the new incoming data and knowledge, but also as a virtual companion, on-board mental trainer.

Finally, in several extended isolation studies as well as aboard ISS we found proof that growing plants in space is necessary not only for nutrition but also to compensate the lack of contacts with nature. Therefore greenhouses could be the crucial element of the future psychological support in the interplanetary flights.

THE POTENTIAL ROLE OF NITRIC OXIDE IN THE MAINTENANCE OF RIBOSOME BIOGENESIS IN UNLOADED RAT SOLEUS MUSCLE

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Nitric oxide II (NO) is considered to be one of the key regulators of catabolic and anabolic processes in skeletal muscle. However, its role in regulation of translational capacity (ribosome biogenesis) in skeletal muscles under mechanical unloading is poorly understood. Therefore, the current study was aimed to determine the potential contribution of nitric oxide to maintaining translational capacity in rat soleus muscle under hindlimb suspension.

Wistar rats were randomly divided into the following groups: vivarium control (C); 7-day hindlimb suspension (7HS); 7-day hindlimb suspension accompanied by intraperitoneal injection of L-arginine (NO donor) (A); 7-day hindlimb suspension along with intraperitoneal injection of L-arginine and intramuscular injection of L-NAME (inhibitor of NO-synthase) (L); 7-day hindlimb suspension together with injection of glycogen synthase kinase 3 (GSK-3β) inhibitor (G). The rats were injected with puromycin 30 min prior to muscle collection in order to assess the rate of muscle protein synthesis (MPS) *in vivo* (SUnSET technique). Puromycin-truncated peptides and GSK-3β content in the whole cell lysate were analyzed by Western blot. The level of mRNA expression of both transcription factor c-MYC and 45S pre-rRNA was determined by RT-PCR. 18S rRNA and 28S rRNA contents were determined by 1.2%-agarose gel electrophoresis.

SUnSET measurements revealed a significant decrease in MPS following both 7 days of hindlimb suspension and 7 days hindlimb suspension with L-arginine and L-NAME administration. There was no statistically significant difference between the C, L and G groups regarding MPS in rat soleus. The same pattern of distinctions between the groups was shown for phospho-GSK3β (Ser9) and the markers of ribosomal biogenesis such as 18S and 28S rRNAs, 45S pre-rRNA and c-Myc.

The findings of the present study suggest that the key markers of ribosome biogenesis as well as the rate of protein synthesis in rat soleus muscle under hindlimb suspension are regulated by NO-synthase activity.

The study was supported by the RFBR grant # 19-015-00089.

CHANGES IN THE PROFILE OF PROTEINS ASSOCIATED WITH THE FUNCTIONS OF THE CARDIOVASCULAR SYSTEM IN SPACE AND GROUND-BASED MODEL EXPERIMENTS

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Cardiovascular proteomics is one of the most rapidly developing areas of proteomic research in space medicine. It is important to clarify the role of some protein signaling molecules of the proteome of biological fluids depending on the state of cardiovascular activity since the features of the proteome correlate with the functional and structural characteristics of the cardiovascular system. On the other hand, autonomic and humoral regulatory mechanisms play a decisive role in maintaining the functional state of the body in the process of physiological adaptation, in connection with which it is relevant to study the processes occurring at different levels of the cardiovascular system and their reflection in the proteomic composition of biological fluids of the human body.

We analyze the change in the profile of proteins associated with the cardiovascular system in the urine of cosmonauts, as well as volunteers participating in ground-based model experiments. As an integral characteristic for assessing the current functional state and physiological homogeneity of the group, we use heart rate variability (HRV), which reflects the total effect of regulation, and autonomic homeostasis. Depending on the type of autonomic regulation, we analyze the proteomic response associated with the cardiovascular system under simulated or real conditions of space flight.

We have established a relationship between the characteristics of the autonomic regulation of the heart rate and changes in the urine proteome in cosmonauts who have performed long-term space flights. Proteins CDH13, MUC1, COL6A1, HMCN1, SEMG2, SH3BGRL3, TTR, and IPSP play a homeostatic role in cosmonauts with different types of cardiovascular regulation. The concentrations of these proteins differ significantly between groups of cosmonauts, with a predominance of parasympathetic and sympathetic modulating influences.

The set of biochemical parameters, unidirectionally changed with these proteins, also different in classified groups. In a group with a sympathetic predominance: DBIL, K+, Ca changed unidirectionally with COL6A1, DBIL, K+ – with MUC1, and UA, Fe, CK, K+ – with CDH13. In a group with parasympathetic predominance: K+, Fe changed unidirectionally with COL6A1, AMS, CK, AST, UA, IP, GLU, ALP, Ca – with MUC1, and TIBC, TF, GLU, GGT - with CDH13.

In experiments with «dry» immersion mathematical and bioinformatics analysis identified proteins that are associated with autonomic regulation of the cardiovascular system in the total protein aggregate. The kit included TRFE, AXL (UFO), SECTM1, ACPP, MXRA8, CADM4, IGHA1, LGALS3BP and BTD. For the first time, the associations of protein markers of autonomic regulation of the heart rate were studied. On the basis of proteomics data, the parameters of physiological regulation of heart rate in the urine proteome of young healthy men are described.

To identify risks in manned expeditions into deep space, it is necessary to search for biomarkers of cardiac activity both in space flight and at the stage of post-flight rehabilitation. We hope that our research can get closer to solving this problem.

The work was carried out within the framework of the basic theme of RAS 64.1 and 65.3 for 2013–2023.

RESULTS AND PROSPECTS OF STUDIES OF CHANGES IN LOWER LIMBS VEINS IN EXPOSURE TO REAL AND SIMULATED MICROGRAVITY

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Reducing of the orthostatic tolerance (OT) of cosmonauts during and after space flight remains an important and still unsolved problem. Most scientists believe that the mechanism of this phenomenon is multifactorial, and the lower limbs veins condition plays an important role.

From 2010 to 2020, a studies of the of the lower limbs veins condition of the cosmonauts in long-term space flights were carried out using occlusive plethysmography. The aim of the work was to identify the effect of microgravity on the condition of the lower limbs veins and to determine the possibility to predict the OT on the basis of the veins studies results. The research involved 28 cosmonauts, 15 of whom participated in two different flights. Venous studies were performed in 47 flights with a duration of 167.8 ± 4.98 days, a total of 285 studies were performed, 90 of them in microgravity.

The following results were obtained

- In 100 % of the studies performed in the SF, there was an increase in the capacity (+45–55 %) and extensibility (+25–40 %) of the lower leg veins compared to the data of pre-flight studies. In most of cases (75 %), there was a 45–50 % decrease in the vein filling rate during the occlusion test compared to the baseline data. However, there were also several cases of increased venous filling rate. The identified changes create the basis for reducing the OT.
- The degree of changes in capacitance, distensibility of the calf's veins and the rate of their fillingt under stepwise-increasing occlusion, and changes throughout the stay in microgravity allow to predict individual orthostatic tolerance (OT) cosmonauts during the 6-month SF.
- Restoration of the lower limbs veins condition, as well as the OT of cosmonauts after the end of the space flight to the pre-flight level indicates the adaptive nature of changes that occur in exposure to microgravity.
- Repeated, after 4 years, participation of 15 cosmonauts in 6-month SF did not reveal the cumulative effect of microgravity on the lower limbs veins condition.

The method of occlusal plethysmography of the lower leg has proven itself well in the conditions of real CP as methodically simple, allowing to stable obtain important information and having good prospects for further use in the conditions of real and simulated microgravity.

This method can be used on Earth both to detect changes in the lower limbs veins when modeling some of the microgravity effects and to evaluate the effectiveness of existing and new measures being developed to prevent orthostatic instability.

The application of this method in combination with ultrasound methods for studying of the cardiovascular system will allow us to obtain more complete information about changes in blood circulation in exposure to microgravity.

INTELLECTUAL PROPERTY COMMERCIAL ISSUES EMBRACING THE TRANSFER OF DATA BETWEEN ORBITAL STATIONS: THE EXAMPLE OF THE LUNAR GATEWAY ORBITAL STATION AND THE INTERNATIONAL SPACE STATION

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The International Space Station represents the first permanent presence of humans in outer space. With the advent of space exploration in the early part of the XXI century, other missions are being planned for humans. The Moon and Mars are

examples of celestial bodies that will feature human presence in the forthcoming years. Such presence may consist of manned permanent space missions in orbiting spacecrafts or in the form of human settlements.

The nature of the so-called Homo Spatialis is evolving and in a not so distant future we will need find that we humans count on different Space Stations orbiting near and not so near celestial bodies. Such missions will help to assist astronauts during their space missions or will serve as permanent space laboratories. The future lunar NASA Gateway Station is a clear example of such human achievements.

But other missions will follow moved by other space players like Russia, China, Europe, the Emirates and new private initiatives.

The communication between different orbital stations could present different characteristics and issues.

Therefore, transfer of data between different locations and different stations orbiting celestial bodies should be understood and follow a guidelines of recommendations issues by space authorities.

Freedom of data distribution, access, use of data should require a collaboration effort between States.

Also Commercial and Intellectual Property rights are important to be preserved, specially, since there are new private players in the space commerce. New researches and discoveries in space will also oblige legislators and Scholars to propound new legislative solutions to protect the intellectual property rights of the inventions in space and the commercial ventures.

EFFECT OF 5-DAY DRY IMMERSION ON THE HUMAN FOOT MORPHOLOGY ASSESSED BY COMPUTER PLANTOGRAPHY AND SOFT TISSUES STIFFNESS MEASURING

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16 participants have been subjected to Dry Immersion model (DI) for 5 days. DI reproduces the space flight factors such as lack of support, mechanical and axial unloading, physical inactivity, elimination of vertical vascular gradient. Long-term bed rest is also associated with similar factors, so the results of the study might be useful for clinical medicine.

Computer plantography and measuring the stiffness of the soft tissues of the foot and superficial muscles of the shin (mm. tibialis anterior and peroneus longus) were performed twice before DI exposure, on the 2nd and 4th days of DI exposure, as well as on the 2nd day of the recovery period. To obtain data on the morphological characteristics of the foot, we used the computer plantography method based on obtaining a graphic image of the supporting surface of the foot. Graphic data processing was performed using a program that was specially written for this study; its algorithm is based on the method of measuring the morphofunctional characteristics of the foot provided in the Russian Federation patent № 2253363 (Gavrikov K.V., 2005). To assess the transverse stiffness of soft tissues we used a Myoton-Pro device (Myoton, Estonia). The measurements were made at 4 points. Two points were located on the foot: the first one – laterally from the head of the first metatarsal bone, the second one – laterally from the junction of the first metatarsal bone with the medial cuneiform bone. Two points were located in the projection of two antagonist muscles: the first one - in the projection of m. peroneus longus, the second one – in the projection of m. tibialis anterior.

DI exposure effects the parameters under study in two ways: by raising the longitudinal arch and by flattening the transverse arch, which is accompanied by a decrease in the soft tissues stiffness of the foot and superficial muscles of the shin. Note that the influence of these factors on the longitudinal arch of the foot was more pronounced. For example, on the 2nd day of DI, the longitudinal arch of the foot became higher, as indicated by a reliable decrease in the flatfoot coefficient k by 2.32 ± 0.97 % ($p < 0.05$). At the same time, a lowering of the transverse arch of the foot was indicated by a reliable increase compared to the baseline values in the AB segment (the distance between the extreme points of the metatarsus on the side of the big toe and the little toe) by 2.09 ± 0.86 % ($p < 0.05$).

The work reveals the phenomenon of compensating the longitudinal arch state by changing the characteristics that reflect the transverse arch state. The results of the study for the first time demonstrate the correlation of the foot morphological characteristics with a decrease in stiffness of mm. peroneus longus and tibialis anterior.

The study was supported by a grant from the Russian Science Foundation No. 19-15-00435.

EMOTIONAL STATE DYNAMICS AND ITS ASSESSMENT WITH SUBJECTIVE AND OBJECTIVE METHODS IN SIRIUS-19 EXPERIMENT

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In long-term isolation experiments, the crew, similarly to long-term space flights, is affected by such negative stressful factors as sensory deprivation, monotony, social isolation, limited resources, off-nominal situations, etc. According to Russian

Mission Control Center (MCC) psychological monitoring group observations of space crews, irritability, cumulating fatigue, sleep disorders, crew mistakes were detected inflight. POMS (Profile Of Mood State) scale has traditionally been used by International psychological space community to assess subjective perception of changes in the emotional state in space flights and isolation experiments. It is also known from Kanas study (2004) that Russian cosmonauts tend to give socially desirable answers to the questionnaires. Data processing technologies development allows to add to the psycho-emotional status observation such a behavioral tool for facial expression analysis as FaceReader software (Noldus). The purpose of this study was to compare subjective and objective assessments of the emotional state of the international mixed gender crew in the SIRIUS-19 experiment.

Six subjects participated in 120-days isolation study: 3 men, 3 women; among them 4 Russians, and 2 US citizens. POMS scale was performed 2 times during baseline period and 16 times during isolation (weekly). FaceReader software (version 7.1) was used to analyze video recordings of subjects' facial expression during daily planning conferences' (DPC) with MCC twice a day.

According to FaceReader data, half of the crew had a general decrease in their emotionality during communication with MCC throughout isolation. These changes can be caused by cumulative effect of sensory deprivation and monotony. One subject demonstrated the increase of negative emotions level; one subject – increase of the positive emotions. For all test subjects, the duration of morning and evening DPC sessions became shorter, which indicates a decrease in the need of data exchange as a general tendency of crew adaptation to isolation conditions (Gushin, Shved, 2018). POMS results demonstrated that most of the subjects throughout the isolation denied the presence of any negative changes of the emotional state. For example, on the «Anger-Hostility» subscale, 98 % of the results were zero for 5 subjects; on the «Fatigue-Inertia» and «Depression-Dejection» subscales, 95 % and 98 % of the results were zero for 4 subjects. This has been observed for Russian and American isolation participants.

We can conclude about discrepancy in subjects' perception of their emotional state and the data obtained by the analysis of their facial expressions. This may be explained by crew members' motivation peculiarities, their ability to reflect emotions, or social desirability bias.

The study was supported by the Ministry of Science and Higher Education of the Russian Federation under the agreement No. _075-1502020-919 from 16.11.2020 about the grant in the form of subsidy from the federal budget to provide government support for the creation and development of a worldclass research center «Pavlov Center for Integrative Physiology to Medicine, High-tech Healthcare and Stress Tolerance Technologies».

EVALUATION OF IONIZING RADIATION EFFECTS AND MITIGATION TECHNIQUES FOR INFLATABLE SPACE HABITATS IN DEEP SPACE MISSIONS

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The major sources for ionizing radiation in space are Solar particle events, Galactic cosmic rays and trapped particles in Van-Allen belt. Solar Particle Events (SPEs) consist of highly energetic proton-electron gas which are ejected sporadically from the Sun at its peak solar activity. Galactic Cosmic Radiation (GCR) consists of approximately 85 % alpha particles, 14 % Helium nuclei, 1 % heavy nuclei and some beta particles. These highly energetic particles are formed by energy deposition into them by supernovae remnants and accelerated to near relativistic speeds. Maximum galactic radiation is observed during a solar minimum, when Sun's magnetic field is at its minimum, while the minimum radiation levels occurs during solar maximum. But due to highly energetic events during solar maximum, (SPEs), the electron and proton flux levels may increase drastically for a short time. This large level of ionizing radiation is harmful for the human body and harmful for electronics.

In this paper, we propose to model the interaction between ionizing radiation in deep space, spacecraft structure and its biological implication. The shield design should also be able to handle heavy nuclei from Galactic Cosmic Radiation. It should also be able to attenuate radiation flux from solitary SPEs. Thus, a reliable model is required to predict and protect crew in such events.

Shield Model. The shield model comprises of the geometry of the shield, specifically the inner and outer structure makeup for the proposed space habitat. Based on the material of construction used in different sections the absorbed dose is arrived.

Shield Transmission Model. The shield transmission model is an indigenous 1 dimensional model developed for a multi layered shield against an incident source of protons, electrons and heavy nuclei. This gives the absorbed dose per layer. Shield transmission characteristics are given by Boltzmann transport equations, as input to the biological model. This yields the flux density per layer of particles of varying energies, taking into account collisions and secondary particle emissions produced as result of these collisions.

Using the Boltzmann Equation for radiation transport.

Human Biological Model. The Relative Biological Effectiveness (RBE) is the parameter which is used to quantify effects of radiation on human tissue. RBE varies for different energy sources. It varies from 1 for X- rays to 20 for alpha particles. RBE can also be termed as a quality factor Q.

The internal environment comprises of the cells and tissues of the astronaut. Using the Relative Biological Equivalent of each radiation type, the dose equivalent is found, that gives the biological response of the astronaut to different types of radiation. Further using body tissue transmission characteristics again computed using Boltzmann equation, the radiation received at critical organs like heart, brain, lungs is assessed.

This paper outlines the absorbed radiation levels in a deep space habitat beyond the Earth's magnetic sphere of influence using an indigenous code developed for a multi layered one dimensional shield against an incident particle source of protons, electrons, heavy nuclei to get absorbed dose for each layer. Radiation levels inside the space habitat are used to calculate the dose equivalent faced by the astronaut with and without flight suit and the total ionizing dose for varying mission duration. Absorbed dose per layer is also computed for TransHab configuration, in order to validate the code. Further dose equivalent faced by the astronauts is computed for the ISS configuration for validating the code.

A few wall configurations for the inflatable space habitat are proposed in order to reduce the radiation dose absorbed. A trade-off between mass increase and dose reduction is performed to select the best configuration.

Passive shielding thickness required is also computed for protection against solar particle events, for the deep space habitat configuration. In order to reduce the mass to be carried for radiation protection and increase payload capacity, especially in deep space missions, an active radiation shielding methodology is proposed.

DYNAMICS OF HUMAN NEUROPHYSIOLOGICAL CHARACTERISTICS UNDER THE INFLUENCE OF A HYPOMAGNETIC ENVIRONMENT

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The assessment and prediction of the reliability of the professional activity of a human operator when performing complex tasks is based not only on the analysis of the quality parameters of the operator's activity, but also on the indicators of the cognitive and physiological functions of the operator performing this activity. The systemic response of the organism, ensuring its adequacy to the requirements of the activity, is defined as a functional state. There is a functional state of operational rest, fatigue, psycho-emotional excitement, etc. The most optimal realization of human cognitive functions is carried out in a state of operational wakefulness with a balance of the processes of excitation and inhibition. It is possible to assess the success of the implementation of cognitive functions using various types of psychological tests. The functional state of the brain is assessed by the relationship between the processes of excitation and inhibition in the central nervous system by electroencephalography.

The purpose of the experiment is: to assess the dynamics of the level of the functional state of the brain on the scale of inhibition-excitation in a hypomagnetic environment.

During the experiment, a computerized complex for polygraphic research was used - an electroencephalograph-analyzer «ENTSEFALAN-EEGA-19/26» (MTD, Medicom, Taganrog), which allowed monitoring, recording and viewing EEG, displaying and recording EEG signals with high resolution (in the frequency range from 0.5 to 70 Hz).

A quantitative assessment of the influence of low magnetic fields on the human body is one of the most debated issues of modern magneto- and heliobiology. Since, in short-term experiments, changes in the magnetic field often do not lead to a visible reaction of the body and a significant change in physiological processes, the actual problem is to assess the prolonged effect of magnetic field variations.

SELF-TRAINING OF THE CREW MEMBERS OF THE SIRIUS 18/19 PROJECT USING THE 6DF SOFTWARE

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The hand controlled docking maneuver is a mission relevant operation of highest importance. Since decades the Russian scientists of the IBMP have run research on this topic. Investigation of the issues of safety and maintenance of sustainable professional skills was started in 1987 as part of the experiment Pilot. The RSC Energia has developed several hard- and software simulators to improve the skill maintenance onboard. These efforts focused primary on realistic work samples and an adequate assessment of performance and psychophysiological load.

The objective of the presented experiment consists in an: application of a self-sufficient docking learning program under simulated flight conditions (isolation). Improvement of methods and development of tools for assessing and predicting the reliability of the professional activity of the operator when performing space relevant operational tasks

The task simulates the manual control of a virtual spherical object in space, which requires the simultaneous processing of six DoF. In the first training sessions the object has to be navigated along a given pathway, indicated by a series of ellipsoid rings. The ellipsoids are semi-transparent to allow the permanent view on the target-object. The path of ellipsoids has to be traversed while looking from inside the moving object out through the camera monitor with a visual adjustment grid (visor). The arrangement of the ellipsoid rings requires rotating around the moved object's axes. The visualized pathway provides guidance to the controlled object from its current position to the target and prevents the trainee from deviating to far outside the approach corridor. At a certain level of education the ellipsoids are omitted. The level of complexity of the tasks is adjustable from a very easy level for novices to an open range in difficulty and complexity. In the present application the functionalities of controllers and flight dynamics reflect the characteristics of the regular Soyuz spacecraft. Performance data are presented for purposes of feedback immediately after finishing a task as a green-yellow-red coded table.

6df software was used in the educational mode for five crew members; the sixth crew member was not involved in the work with the software «6df», as he professionally mastered this skill as a member of the cosmonaut corps.

The average performance at individual levels of difficulty was similar for all participants due to the learning conditions, when a higher level could be passed only if the result of the completed task was sufficient for this. However, the level of difficulty achieved and the learning rate varied greatly among the participants (60, 25, 121, 50, 50).

Obviously, one of the participants performed the tasks much better than the others. He quickly climbed the difficulty levels and reached the highest educational level (60) and could continue with docking on a rotating station, which exceeds the standard requirements. For all other participants, the number of sessions and tasks was not enough to reach the standard 60th docking level. Individual differences in docking maneuver accuracy (Figure 8), processed by statistical analysis using Linear Mixed Model Analysis (LME), MIXED procedure in SPSS, showed that accuracy varied between complex levels as expected [F (number: 16, denum: 908) = 5.974 p = .000] - the more difficult the tasks, the lower the performance, this is tautological.

This version of the software was successfully applied stand-alone during SIRIUS 18/19 and provided reasonably significant individual differences among participants.

NEUROPHYSIOLOGICAL MECHANISMS OF COGNITIVE PROCESSES WHEN PERFORMING OPERATOR TASKS OF DIFFERENT COMPLEXITY

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Operator activity as a special type of activity was formed in connection with the achievements of scientific and technological progress, the development of technical systems and their control systems. This puts forward new requirements for the human operator associated with the reception and processing of information, making responsible decisions in situations with lack of time. An important place is occupied by the development of methods for assessing the psychophysiological state and quality of the operator's activity. The productivity of the human operator is a function not only of knowledge, skills and abilities, but also depends on functional changes in the body and psyche in the process of performing work.

Cosmonauts practice operator skills on the Simulator Complex, which includes, in particular, specialized rapprochement and docking simulators of the Soyuz transport vehicle (Don-Soyuz TMA and Don-Soyuz TMA-2) designed to form and maintain crews manual control skills to maneuver a manned or transport vehicle and its systems during rapprochement, docking, flyby, docking and undocking with another space object. Working out the modes of urgent abandonment of the International Space Station by the crews on two spacecrafts at the same time (integrated operation of two simulators) was trained.

The purpose of the present experiment is to study the neurophysiological mechanisms of cognitive processes when performing complex operator tasks at the stages of a long space flight and after landing.

The model of operator activity is the «Six-degrees-of-freedom (6df)» program that simulates manual control of objects with 6 degrees of freedom with built-in cognitive tasks and a separate program of cognitive tests. The data on the quality of activity are compared with the indicators obtained using the hardware complex «Neurolab-2010». The complex «Neurolab-2010» provides registration of the following physiological parameters: electrocardiogram; pulse wave from the left little finger; skin temperature of the little finger (left); electrocutaneous resistance on the left little finger; as well as recording a speech signal, as well as a set «Neurolab-2010 +», with the help of which EEG recording from 19/8 derivations is carried out using dry active electrodes (sensors), as well as electrooculogram and electromyogram registration.

Considering the results, we can say that one of the crew members has a high level of professional activity, since according to the primary control parameters he showed that throughout all the stages of the experiment, the values of the touch parameters are included in the permissible values. As the experiment progresses, positive dynamics are visible: a reduction in fuel consumption, time to complete a task, as well as a stable level of angles mismatch in pitch, yaw and roll.

In the Sirius Study the EEG registration with dry electrodes was successfully tested, obtaining standard EEG. First application onboard ISS demonstrated the feasibility of the method to use the EEG signal to extract event related potentials, especially

the P300 component. This provides the possibility to assess the free cognitive capacity of operators during the operational task when solving a secondary task. All participating cosmonauts showed excellent docking performance data and the clear occurrence of the P300, indicating their high level of proficiency.

THE EFFECT OF PREVIOUS SPACEFLIGHT ON OTOLITH-MEDIATED OCULAR COUNTER-ROLL IN COSMONAUTS AFTER LONG DURATION SPACEFLIGHT

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Introduction. The otolith system plays an essential role in the estimation of verticality, where an otolith driven eye movement, the Ocular Counter-Roll (OCR), is important to ensure gaze stabilization, as the eyes tilt in the opposite direction to the direction of the head tilt. Long duration exposure to microgravity, as experienced aboard the International Space Station (ISS), will cause a deconditioning of the otolith system. As a result, cosmonauts will experience balance disorders and problems with gaze stabilization after returning on Earth. The aim of this study is to measure the effect of long-term spaceflight on the otolith-mediated OCR, in cosmonauts, with focus on the difference between first time flyers versus frequent flyers.

Material and methods. 44 cosmonaut experiments were performed, first time flyers (1F, N = 14) and frequent flyers (FF, N = 30), were exposed to off-axis centrifugation before and after their 6-month space mission to the ISS. The OCR induced by the Visual and Vestibular Investigation System (VVIS) mini centrifuge was assessed and recorded for 20 seconds at a maximal velocity of 254°/s, out of a total duration of 5 minutes centrifugation. The OCR measurements were further statistically analyzed in SPSS, with $p < 0,05$ as significance threshold.

Results. We found a significant decrease in OCR early postflight (R3/5, three to five days after return) for both the 1F group and the FF group. The post-flight OCR decrease in the 1F group was significantly different from the FF group with a greater reduction in the 1F group. A full recovery was seen nine to eleven days after their return (R9/11).

Conclusion. The FF group suffered less from a deconditioning of the otoliths, because they may have acquired an adaptation from previous space missions, demonstrating a learning effect. The results argue for that for important missions, e.g. to the Moon or Mars, it is more advisable to send experienced cosmonauts or astronauts because they are noticeably less affected by microgravity regarding the vestibular system.

LONG-TERM CNS EFFECTS OF LOW-DOSE GALACTIC COSMIC RADIATION ON WILDTYPE AND ALZHEIMER'S-LIKE MICE

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Background. Space radiation may pose risks to humans in spaceflight and exacerbate predispositions to neurological diseases. Previously, we demonstrated sex-, genotype-, and dose-specific effects of single ion space-like radiation with ^{56}Fe or protons on motor behaviors, psychological state, learning and memory, and amyloid-beta in mice. For example, male wildtype (WT) and Alzheimer's disease-like APPswe/PS1dE9 mice, but not females, showed cognitive deficits 8 months after ^{56}Fe irradiation.

Methods. Mice were irradiated at Brookhaven National Laboratory with simulated 5-ion Galactic Cosmic Radiation (GCRsim) mixed-field beam (protons, ^{56}Fe, ^{16}O, ^{28}Si, and ^{4}He) or gamma radiation. Four-month-old male and female, WT and APP/PS1 mice were divided into 2 cohorts (n=114/cohort) and received sham, 0.5 Gy or 0.75 Gy GCRsim, or 0.75 Gy or 2 Gy gamma radiation. One subset of mice underwent pre-and post-irradiation brain and cardiac MRI scans at 3.5 and 11.5 months of age, respectively. Another subset underwent behavioral testing at 11.5 months of age. Mice were euthanized at 12–13 months.

Results. While radiation did not affect survival, ~ 50% of female APP/PS1 mice died prematurely as observed previously by us and others. By MRI (n=3-4 mice/group), we saw increased ventricular volume in male WT sham, female WT 0.5 Gy, and male APP/PS1 0.5 and 0.75 Gy GCRsim mice, but no changes in gamma mice. Hippocampal volume was increased in male WT sham, male APP/PS1 0.5 and 0.75 Gy, male WT 0.75 Gy GCRsim mice, as well as in male WT 0.75 Gy and female WT 2 Gy gamma mice. Cortical volume was reduced in male WT sham mice and male and female WT 0.75 Gy GCRsim mice, as well as in female WT 0.75 and 2 Gy gamma mice and male WT 0.75 Gy gamma mice. Radiation had no effect on cardiac ejection fraction, stroke volume index, or left ventricular wall thickness. Behaviorally, male WT 0.75 Gy GCRsim and gamma

2 Gy mice showed cognitive impairment in the Spatial Novelty Y Maze. 2 Gy gamma irradiation reduced sensorimotor gating in WT females compared to shams. 0.75 Gy GCRsim worsened coordination on the rotarod in APP/PS1 females, though an opposite trend was seen in APP/PS1 males. Similarly, 0.5 Gy GCRsim improved endurance of APP/PS1 males on the Wire Hang test compared to shams. Neither GCRsim nor gamma irradiation influenced fear memory, startle reactivity, or anxiety-like or depressive-like behaviors. Amyloid-beta levels in brain homogenates (measured by ELISA) were unchanged by radiation exposure but, as expected, were higher in female than male APP/PS1 mice.

Conclusion. Overall, our results demonstrate that radiation worsened spatial memory in WT male mice, consistent with our previous findings with ^{56}Fe irradiation, and suggest that low doses of space-like radiation have sex-specific, long lasting effects on brain measures.

CLINICAL AND MORPHOLOGICAL PORTRAIT OF CATARACT IN DYNAMICS FROM THE UV INDEX ACCORDING TO PAKISTANI STATISTICS

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Relevance. The exploration of outer space beyond the near-earth orbit is associated with the development of new technologies for medical support, which are based on the study of the somatic status and adaptive reserves of the body under the action of extra orbital factors of outer space.

The ultraviolet spectrum (UV) of optical radiation in outer space is a potentially dangerous extra orbital factor. The UV spectrum includes a wavelength range from 100 to 400 nm. With a decrease in the wavelength of the UV spectrum (UVB), the energy of the radiation quanta increases, leading to the destruction of molecular bonds in organic compounds. It is assumed that in the absence of a protective ozone layer against UV during a long space flight and on the lunar surface, the risk of UV damage to the visual system will increase significantly.

The increase in the instability of the ozone protective layer in the Earth's stratosphere observed over the past 10 years leads to an increase in the concentration of ultraviolet waves from 280 to 315 nm (UVB). This process is typical primarily for countries with a high UV index (more than 5), with increased seismic activity, subtropical and tropical climatic zones, which include Pakistan.

Statistical analysis of the clinical and morphological features of the development of cataracts in Pakistani residents made it possible to identify both the morphological specificity of UV damage to the visual system and to assess the level of biological resistance of eye tissues to UV exposure.

Objectives. Conduct a statistical analysis of the clinical and morphological features of the development of cataracts of Quetta residents, taking into account age, gender characteristics, to assess the level and nature of biological resistance of eye tissues to UV exposure.

Materials and methods. According to the helper hospital Quetta Baluchistan a comprehensive analysis of statistical data for the period from 2010 to 2020 was carried out. registration of cases of cataracts of the eye, the presence of dystrophic complications of the anterior and posterior segment of the eye, refraction of the eye, the nature of the postoperative period of convalescence, taking into account age and gender characteristics.

Results. Based on the results of a comprehensive statistical analysis, a clinical and morphological «portrait» of cataracts of the residents of the Baluchistan province was obtained. Pakistan.

The increase in UV radiation directly correlates with the frequency of registration of cataracts. Gender and age characteristics of this pathology were revealed. A characteristic feature of the morpho-functional ocular status in cataracts in people under the age of 50 was the presence of a specific form of corneal dystrophy, destruction of the pigment epithelium of the iris and retina.

AUTOMATION OF ONBOARD CREW HEALTH MONITORING SYSTEM USING ARTIFICIAL INTELLIGENCE ALGORITHMS

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Crew health monitoring is a mandatory crew safety requirement for human space flight mis-sions. Crew health monitoring for astronauts include monitoring set of human physiological pa-rameters such as heart beat, respiration rate, oxygen saturation

in blood, electrocardiogram (ECG) etc. using a wearable health monitoring sensors.

ECG waveform is one of the most crucial data for assessing crew health among the battery of health parameters. Often the data obtained from ECG electrodes is synthesised on-board and telemetered down to earth, where a team of doctors/flight surgeons analyse the data and report crew health to mission control.

Deep Learning and neural network architectures are being used widely to cater various chal-lenges at the critical places where lots of resources are required to execute the mission especial-ly in case of on-board applications.

In this study, artificial intelligence algorithm is proposed for extracting and learning the fea-tures from ECG data acquired from the crew health monitoring electronics. The synthesised ECG wave form will be analysed using an ensemble of both machine learning and deep learning mod-els.

Developed and trained working model for ECG data will enable automated monitoring and alert generation thereby reducing human workload.

Outcome of this study can also be extended for resolving the challenges of crew health moni-toring and status reporting in deep space missions where limitation exist with regard to data transmission rates and latency.

SUPPORT AFFERENTATION COREGULATES SLOW MYOSIN EXPRESSION AND MITOCHONDRIAL BIOGENESIS AND PREVENTS UNLOADING-INDUCED FATIGUE IN RAT SOLEUS MUSCLE

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Real or simulated weightlessness cause slow-to-fast fiber-type transformation and decline of mitochondrial biogenesis, that lead to enhanced muscle fatigue of the postural hind limb skeletal muscles. Support afferentation restoration under conditions of simulated weightlessness leads to prevention of slow myosin mRNA transcription downregulation. Some literature data suggest that slow myosin mRNA expression restoration may lead to stabilization of slow oxidative fiber-type and enhance fatigue resistance (Quiat et al, 2011).

The aim of this investigation was to test the hypothesis that the support afferentation restoration during rat hindlimb unloading increases fatigue resistance and mitochondria-related genes expression in postural soleus muscle, and to identify the mechanisms of such prevention.

Male Wistar rats were divided into three groups (n=8): vivarium cage control (C); 7 day hindlimb unloading (7HS); 7 day hindlimb unloading with plantar mechanical stimulation (7HS+PMS). Animals from 7HS+PMS group for 4 hours a day all along the experiment underwent support stimulation of the soles of the feet according to the scheme simulating the normal walking of the animal. The index of fatigability of the soleus muscle was measured as force decrease after 20 tetanic isometric contractions (40 Hz, 20 V, 3 sec). Expression of slow myosin (MyHC I(β)), mitochondrial biogenesis genes (including PGC1α), and expression of myh7b, microRNA-499 and SOX6 were analyzed using RT-PCR. The level of phosphorylation of kinase GSK-3β in the total protein fraction was analyzed by Western blot.

After 7 days of hindlimb unloading, we observed a significant decrease in the soleus muscle fatigability index by 40% compared to control, while in the 7HS + PMS group, there were no significant differences from control. Decreased expression of slow isoform of MyHC I(β), PGC1α, COXI, COXII and mitofusins 1 and 2 and downregulation of mir499/myh7b were observed after 7 days of HS, as well as GSK-3beta activation. All these changes were prevented in the group with PMS. Both myh7b/mir-499 upregulation and GSK-3β inactivation may contribute to PMS-induced prevention of mitochondria-related genes expression decrease.

Thus, supporting mechanical afferentation during functional unloading prevents an increase in fatigability of the soleus muscle, which is accompanied by the prevention of a decreases of mitochondrial biogenesis and slow-type myosin genes.

The study was supported by Basic research programme of IMBP.

STUDY OF THE EFFECT OF A RADIATION-CHEMICAL FACTOR ON THE INTESTINAL MICROBIOME OF RATS

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Introduction. In the modern world, the number of stressful influences and unfavorable environmental factors has increased, accompanied by a sharp violation of the microbial ecology of the host organism. Due to the influence of external conditions, dysbiosis of various etiologies is formed, conditionally pathogenic microflora and immunodeficiency conditions arise, in which the body's resistance to exogenous and endogenous infections decreases, affecting ENT organs, surface integuments and

internal mucous membranes of a living organism. Due to the prevalence of opportunistic microflora under the influence of environmental stress factors, medical risks arise, leading to the need for the development, use of preventive measures, as well as more thorough and in-depth control over the state of the body. Early studies showed that environmental factors such as temperature changes, exposure to radiation, etc., play an important role in the formation of the microbial community inside and outside a living organism. In the conditions of a long space flight, a living organism is affected by various unfavorable factors, one of which is radiation-chemical.

The aim of the study was comprehensive assessment of rat intestinal microflora under the influence of radiation and chemical contamination factor.

Materials and methods. The experiment reproduced the conditions of fractionated exposure to gamma irradiation in a total dose of 245 cGy. Irradiation was performed in 10 fractions of 49.9 cGy (effective dose 24.5 s Gy) 2 times a week for 16 hours. The chemical action of the factor was carried out in combination using a mixture of chemicals. The biological object of the study is male Wistar rats. Seven groups (control and experimental) were formed, four biological objects in each. The study of the intestine of rats was carried out on the 0th, 14th and 90th days after exposure to factors. A microbiological assessment of the quantitative and species composition was carried out by means of the passage of the biomaterial on selective nutrient media.

Results and discussion. The study of the quantitative and species composition of the rat intestinal microbiome showed that the species diversity of conditionally pathogenic microflora, both in the control and in the experimental groups, was significant, so in the experimental groups after exposure to the 0th, as well as on the 14th day there was a sharp a decrease in the number of protective (bifidobacteria, lactobacilli, E. coli, etc.) and an increase in the number of opportunistic groups of microorganisms (Staphylococcus spp, Staphylococcus aureus, streptococci, enterococci, yeast-like fungi, etc.), which confirms the negative impact of irradiation combined effect of factors on the intestinal microbiota of rats. After a long recovery period (90 days), the probiotic index and the composition of microflora are restored to normal, the species composition changes in the intestine, the number of yeast-like fungi, staphylococci, streptococci decreases, and the level of E. coli, bifidobacteria and lactobacilli normalizes.

Conclusion. The results obtained allowed us to calculate the eubiotic index. In the course of the study, criteria of positive (an increase in the number of protective groups of microorganisms, a decrease in the number of opportunistic microorganisms, stabilization of the quantitative composition of microorganisms of protective groups at the normal level, stabilization of the quantitative composition of microorganisms of conditionally pathogenic groups below normal) and negative (an increase in the number of conditionally pathogenic groups microorganisms, a decrease in the quantitative composition of microorganisms of protective groups, stabilization of the quantitative composition of microorganisms of protective groups at a level below normal, stabilization of the quantitative composition of microorganisms of conditionally pathogenic groups at a level above normal. The data obtained can be taken as a basis for research on the development of means for the prevention of dysbiotic disorders when the crew members are exposed to space flight conditions in manned lunar expeditions and interplanetary missions.

THE HUMAN RESEARCH PROGRAM SUITE OF INTEGRATED ONE-YEAR MISSION EXPERIMENTS (CIPHER): DESCRIPTION AND INTEGRATION

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The NASA Human Research Program has implemented a set of ISS Standard Measures: a standardized set of assessments to be performed on all consented ISS crewmembers, to provide a common set of measures that span the range of responses of interest to HRP. In 2018, in order to augment these measures and specifically consider effects of longer-duration missions, HRP solicited several additional studies. Ten proposals were selected. Five additional projects were added from international partner agencies, for a total of 15 individual projects. These form the CIPHER project: Complement of Integrated Protocols for Human Exploration Research.

- Preventive Medical Ultrasound Investigation of Organs Potentially Affected by Prolongated Exposure to Microgravity (Philippe Arbeille, University of Tours).
- Telomeres and the One Year Mission Project (Susan Bailey, Colorado State University).
- Temporal Nature of Cognitive and Visuospatial Brain Domain Changes during Long-Duration Low-Earth Orbit Missions (Mathias Basner, University of Pennsylvania).
- Time Course of Spaceflight-Induced Adaptations in Bone Morphology, Bone Strength and Muscle Quality (Mary Bouxsein, Beth Israel Deaconess Medical Center).
- The Effect of Long-Duration Space Flight on Bone Microarchitecture and Strength Using Three-Dimensional High-Resolution Imaging (Steven Boyd, University of Calgary).

- Temporal Changes in Astronauts Muscle and Cardiorespiratory Physiology Pre, During, and Post Spaceflight (Meghan Downs, JSC).
- Manifestations of Spaceflight-Induced Sub-Clinical Cardiovascular Disease as a Long-Term Health Risk (Richard Hughson, University of Waterloo).
- Coronary Anatomy and Physiology During One Year in Space (Ben Levine, University of Texas Southwestern Medical Center at Dallas).
- Joint Health During a 1-Year Mission to the ISS - An Assessment of Exploration Relevance (Anna-Maria Liphardt, Friedrich-Alexander-Universität).
- Investigating Structure and Function of the Eye (Brandon Macias, JSC).
- The Effect of Long-duration Spaceflight on Renal Tissue Injury (Chie Matsuda, Japan Aerospace Exploration Agency).
- Validation of Fitness for Duty Standards Using Pre- and Post-Flight Capsule Egress and Suited Functional Performance Tasks in Simulated Reduced Gravity (Jason Norcross, JSC).
- Neuro-Vestibular Examination During and After Spaceflight (Millard Reschke, JSC).
- Evaluating Resistive Exercise as a Long-term Countermeasure for Spaceflight-Induced Bone Loss Using Calcium Isotopes (Stephen Romaniello, Arizona State University).
- Assessment of Otolith Function and Asymmetry as a Corollary to Critical Sensorimotor Performance in Missions of Various Durations (Mark Shelhamer, Johns Hopkins University).
- Characterizing the Baselines of Sleep Quality, Cognitive/Operational Performance, Immune Function, and Intracranial Fluids for Deep Space Expeditions (Quan Zhang, Massachusetts General Hospital).

The overall goal of this integrated study is to determine if there are systematic differences in the human response to space flights of different durations, up to one year. Much is understood about the response to six months in space; similar results at one year would lend confidence that the time course of each response is well characterized.

Proactive measures are being taken to integrate the individual projects to develop a cross-disciplinary time course of changes. This integration effort consists of, inter alia, identifying conflicts and synergies between projects, and analyzing data for cross-disciplinary correlations and connections across projects.

PLANTAR AFFERENT STIMULATION EFFECTS IN POSTURAL MUSCLE. LESSONS FROM HUMAN AND RAT STUDIES

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According to the theory of Inessa B. Kozlovskaya, under conditions of the Earth gravity, the human body is affected by the action of the axial loading and support reaction force (which is directed to the body surface interacting with the substrate). The results of the comparative analysis of data obtained in the dry immersion and bedrest studies allowed to suggest the hypothesis on the prominent role of the support afferentation in the maintaining the activity of slow, tonic motoneurons. I.B. Kozlovskaya and her followers suggested that under the support withdrawal the support afferentation was sharply declined and provided the loss of depolarization wave generation by spinal motoneurons, which stopped tonic charging. It is followed by switching off the slow-twitch muscle fibers, loss of their stiffness, shortening of muscle fibers, a reduction in muscle protein synthesis and an increase in protein degradation. The justification of this hypothesis became possible when the methodology of the plantar mechanical stimulation during gravitational unloading was implemented into the experimental work in human and animal simulated microgravity studies. It turned out that (1) the support mechanical stimulation evoked the activity of the slow motor units even under gravitational unloading [Shigueva et al., 2015], (2) the support stimulation prevented a reduction in muscle intrinsic stiffness and cytoskeleton destruction including giant sarcomeric titin and nebulin proteins and intermediate desmin filaments [Grigoriev et al., 2004; Ogneva et al., 2011; Tyganov et al., 2020; Shenkman et al., 2004], (3) the support stimulation even at the early stages of the atrophy development prevented the suppression of the anabolic signaling and hyperactivity of catabolic signaling as well as the slow-to-fast fiber transformation in the postural muscle [Sharlo et al., 2019; Tyganov et al., 2019, 2020]. (4) It was also shown that different signaling indices require different number of support stimulation bouts for their maintaining and (5) support-dependent maintaining of anabolic parameters, cytoskeletal proteins and slow myosin expression requires NO-triggered signaling activities. Thus, the hypothesis on the role of the support afferentation in maintaining structure, mechanical properties and signaling pathways of the postural muscle was confirmed.

The study was supported by the Program of the Basic studies of SSC RF – IBMP RAS (topic 65.3) and by the Russian Foundation for Basic Research (grant #17-29-01059).

EFFECTS OF HIGH FREQUENCY ELECTROMYOSTIMULATION ON CHARACTERISTICS OF THE ACCURACY OF CONTROL OF MOVEMENTS UNDER DRY IMMERSION CONDITIONS

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The aim of the work was to study the effect of high-frequency electromyostimulation (EMS) on the activity of motor units (MU) when performing the task of maintaining a small voluntary effort and on the accuracy characteristics of voluntary leg movements under conditions of support unloading.

In order to reproduce the physiological effects of microgravity, we used the ground model developed at the Institute of Biomedical Problems – Dry immersion (DI), which provides a state of deep support deprivation. The studied function was the order of recruitment of the MU of the shin extensor muscles (m.soleus and m.gastrocnemius) in the task of maintaining an isometric effort of plantar flexion of small amplitude. In order to study the accuracy characteristics of voluntary leg movements, we used the task of force gradation when performing single-joint isometric movements of plantar flexion - to distinguish the values of muscular efforts when performing sequentially increasing efforts from minimum to maximum with a minimum difference in the intensity of adjacent movements. The study was conducted under conditions of 5 and 7-day DI with participation of 18 volunteers.

The results of the studies confirmed the assumption that under 1G gravity the maintenance of a small force in the shin extensors is provided by activity of small motor units that primarily precede the execution of movements, structural features of which provide them a greater sensitivity to excitatory influences. Under DI conditions the order of MUs' recruitment in the shin extensor muscles clearly changed: the number of MUs' involved in the motor task with high values of interspike intervals significantly increased. At the same time, the accuracy properties of the studies muscles decreased, which was manifested in a decrease in the total number of distinguishable efforts and an increase in the differential threshold. A tendency towards a decrease in the absolute threshold of effort was recorded on the 5th day of DI. At the same time, the number of erroneous movements during DI effect gradually decreased further.

It is obvious that under these conditions, the question of the possibility of correcting postural functions by other afferent inputs, in particular proprioceptive, becomes important. This question lays in the basement of the study, in which during support deprivation by DI, in order to increase the excitability of proprioception, daily EMS of the muscles of the right and left lower extremities was used using an apparatus «Amplidin-EST». The use of daily EMS during DI exposure prevented a change in the order of MUs' recruitment in the performance of the motor task, which indicates the significant role of proprioceptive muscle information in the development of hypogravitational motor syndrome. As expected, the use of additional receptor stimulation was also effective in eliminating the concomitant effects of microgravity – reducing the accuracy properties of leg muscles.

With the support by the Ministry of Science and Higher Education of the Russian Federation in the framework of agreement № 075-1502020-919 from 16.11.2020.

STUDY OF THE EFFECTS OF LOW-FREQUENCY ELECTRICAL MYOSTIMULATION DURING 5-DAY DRY IMMERSION ON THE HYPERREFLEXIA AND VERTICAL BALANCE

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It has been shown that space flights (SF) even of a short duration are followed by the alterations in sensory-motor system, such as hypogravitational hyperreflexia and vertical stance disturbances (Kozlovskaya, 1981). To avoid the negative effects of SF factors different countermeasure approaches are used. One of them is electromyostimulation (EMS) which allows to maintain force-velocity properties of leg muscles. However, the impact of EMS on the system of postural regulations has not been sufficiently studied yet.

In this study we investigated the effects of EMS training conducted during the 5-day Dry Immersion (DI) on the vertical stance characteristics and the level of hyperreflexia.

During DI, we performed electrical stimulation of the leg muscles using low-frequency EMS-stimulator. The signal frequency was 25 ± 1 Hz; stimulation (1 sec. of stimulation, 2 sec. of rest) carried out daily for 4 hours. Subjects voluntary chose the stimulation amplitude so as to provide maximum muscle contraction, not accompanied by pain.

To register postural characteristics stabilometric platform was used. The center of pressure displacement velocity (COP) and the average amplitude of COP deviation were registered; the ratio between baseline and post-DI values were analyzed. The subjects stood on the soft support (foam pad 20 cm thick) with eyes closed for 40 s. The study was performed before DI and on the day of DI completion.

To evaluate the hyperreflexia effects before and after DI the thresholds and amplitudes of transcranial and transspinal magnetic stimulation evoked potentials (Nosikova, 2021) of mm. soleus and gastrocnemius were registered.

The analysis of EMS selected amplitude showed that the subjects divided into 3 subgroups: (1st – not higher than 32mA and 26 mA, 2nd – not higher than 20mA and 15mA, 3rd – not higher than 17mA and 15mA, for hip and shin muscles, respectively).

Interrelation between EMS amplitude and stabilographic parameters changes after DI accomplishment was revealed. However, this tendency wasn't significant.

During the analysis of the evoked potentials we found the significant dependence between the decrease of m. soleus evoked responses amplitude and EMS amplitude ($p = 0,0191$). Amplitude of m. gastrocnemius responses also decreased. Notice, that significant changes were registered mostly for transspinal evoked potentials, that can tell us about peripheral mechanisms changes, caused by the EMS. Thresholds of potentials increased together with increase of EMS amplitude, but these changes were not significant.

It is important to note, that decrease of the evoked responses thresholds and increase of their amplitude is the natural consequence of the support withdrawal. To all appearances it helps sensory system to maintain vertical balance. Decreased thresholds help to react earlier to the vertical stance disturbance, raise of the amplitudes helps to maintain appropriate force by the atonic muscles. The results of the study allow to suggest that the intensive EMS training without coordination training can dysregulate the adaptive processes of postural control after landing.

Study is supported by the Russian Federation Ministry of Science and High Education №_075-1502020-919.

THE INVESTIGATION OF COMBINED IMPACT OF IONIZING RADIATION AND HYPOGRAVITY ON CENTRAL NERVOUS SYSTEM AS A KEY PROBLEM OF DEEP SPACE MISSIONS SAFETY

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In the deep space missions associated with going beyond the Earth's magnetosphere, one of the main limiting factors is space radiation. In combination with other space flight factors (SFF), their impact can lead to disorders of the functions of the central nervous system (CNS), which are the basis of the operator performance of astronauts. In contrast to the long-term stochastic consequences of radiation exposure (carcinogenesis, cataractogenesis, cytogenetic disorders, shortening of life expectancy, etc.), the ergonomic risk caused by possible violations of the operator activity of astronauts is associated with a threat to their lives directly during the flight. The main danger is represented by galactic space rays (GSR) – high-energy protons and heavy ions with energies in a wide range, up to ultrahigh energies of the order of 10^{20} MeV. It is extremely difficult to protect yourself from such high-energy radiation in the conditions of a spacecraft. This makes it necessary to revise the paradigm of radiation safety for interplanetary flights, in which functional disorders of the CNS become the main critical factor.

The second most important SFF is microgravity. There is reason to believe that these two factors may act in a number of cases in a one-way manner. This determines the extreme urgency of studying the neurobiological effects of these factors. At the same time, there is practically no work in this area.

In our laboratory, a number of unique experiments were conducted using the methodology developed by us for the most adequate modeling of these factors in a ground experiment on rats and primates. It includes synchronous combined exposure to long-term gamma-radiation and simulated microgravity: anti-orthostatic suspension (ANOS) for rats and anti-orthostatic hypokinesia (ANOH) for primates, followed by irradiation of the animals ' heads with high-energy protons or ^{12}C carbon ions. In experiments on rats, the neurobiological effects of such effects were studied at all levels of the CNS organization – from molecular to integrative (animal behavior).

It is shown that after combined exposure to ANOS of different durations (7, 14, and 30 days), prolonged gamma irradiation, and proton irradiation, the main components of motor and exploratory activity in animals are restored fairly quickly after combined exposure to ANOS, and the effect of ANOS prevails in the formation of the emotional and motivational basis of behavior in the «open field» test. When combined impact, the studied factors had a much more pronounced effect on emotional and motivational processes than on cognitive functions. The most significant disorders were registered at 30-day ANOS, the least – at 14-day ANOS. Thus, 30-day exposure to ANOS and combined exposure to ANOS + radiation disrupts long-term memory; only radiation does not give this effect.

The detected changes in the cognitive functions of animals correlate well with changes in the concentration of monoamines in the brain structures responsible for cognitive and emotional-motivational behavior; at the same time, the combined effects of ANOS + gamma- irradiation + protons, along with the hippocampus and prefrontal cortex, revealed changes in the nucleus accumbens, which is the main integrating structure of the mesolimbic dopaminergic system, which induces motivated behavior.

The study of the molecular mechanisms of the neurobiological effects of synchronous combined effects on the functional responses of the rat CNS of 30-day ANOS, gamma- irradiation, and high-energy proton irradiation (expression of dopamine and serotonin receptors, enzymes, and transporters in key brain structures) in comparison with the study of monoamines

metabolism in these structures showed that the effects of ionizing radiation and ANOS under their combined effects undergo interference interactions, either neutralizing each other, or generating new effects on the monoaminergic neural networks within the studied morphological structures of the brain, which partially neutralize the negative consequences of the isolated action of these factors.

When studying the spectral and amplitude-frequency characteristics of the rat EEG after these impacts, there was a tendency to decrease the average frequency and amplitude within the delta rhythm of the maximum peak of the spectrum. Within the theta rhythm of the maximum peak and minimum peaks, no significant changes were observed.

In experiments on primates (Macaca mulatta) with the combined effect of 7-day gamma irradiation + ANOG + head irradiation with ^{12}C ions, the key factor was the typological characteristics of the higher nervous activity (HNA) of animals: the preservation of cognitive functions in monkeys of a strong balanced type of HNA and their violation in individuals with insufficient plasticity of nervous processes. This was accompanied by a significant decrease in the level of monoamines and their metabolites in the peripheral blood.

RADIATION RISK IN LUNAR MISSIONS: ESTIMATION AND COUNTERMEASURES

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Manned space missions require the adequate monitoring, account and prognosis of exposure to space radiation because of possible negative radiobiological effects on the crew both during the flight (short-term acute effects) and long after the mission is completed. In view of the radiation factor, the flights to the Moon are far more dangerous than the near-Earth orbital flights. Due to the absence of protection provided by the Earth's magnetosphere, the radiation doses from powerful solar cosmic ray (SCR) events can be tens and hundreds times higher than those recorded on the ISS orbit. In case of such SCR events, the flights to the Moon in the periods of radiation environment disturbances place special requirements and demands on forecasting of SCR events during the flight.

The estimations based on the SCR model of the Research Institute of Nuclear Physics, Moscow State University, show that at the predefined level of reliability of 97 % when the probability of exceedance of maximum permissible radiation doses is below 3 %, the expected stay time on the near-Moon orbit or on the lunar surface for humans protected with 10 g/cm2 aluminium shielding should be no more than 1.5 months in the solar activity (SA) maximum and about 1 year in the SA minimum.

The contribution to the dose of heavy charged particles (HZE) during the flights to the Moon is several times higher than during the flights of the same duration on the ISS orbit; hence, the probability of negative effects of GCR on the cognitive functions of astronauts increases, leading to mistakes in operator performance directly during the flight. Further studies in this field are necessary in view of the high uncertainty of radiobiological results obtained in the experiments with animals at accelerators.

For controlling the designed level of reliability in lunar missions, lunar spacecrafts should be equipped with the local (on astronaut's body) and/or additional shielding with a specially selected material on the less protected surface of the spacecraft module. The prototypes of such protective equipment and the experience of flight support in hazardous periods have been already worked through in the ISS Russian Orbital Segment (ROS). A hydrogenous water shield has been successfully used in the ISS ROS for many years. Data from our dose measurements enable an evaluation the efficacy of reducing dose equivalent in the crew cabin using water-based shielding, absorption and production of secondary neutrons included.

For lunar missions, it is necessary to take into account the joint effect of zero gravity, radiation and low magnetic field (hypomagnetic conditions), which is currently understudied. The manned lunar flights with an acceptable level of reliability with respect to radiation safety are possible but require further studies and the development of special technical and organizational measures and means for radiation (and, in a broader sense, medical) safety assurance for the flight crews.

In view of the lack of our knowledge about radiobiological effects of HZE-particles from GCR and powerful SCR events, at the first stage it seems reasonable to limit the duration of lunar missions to 1.5 months. Later on, the duration of lunar missions can be extended as more data on the medical support, methods and means of radiation protection are accumulated.

SIMULATION MODELING AS AN IMPORTANT TOOL FOR THE PRODUCTION OF LIFE-SUPPORT SYSTEMS

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The implementation of long-term autonomous interplanetary space missions to objects of the Solar system predetermines the priority of improving all onboard systems and, in particular, life support systems. One of the main functions of the

integrated life-support systems (ILSS) of an interplanetary manned vehicle is the maintenance of a pre-planned gaseous environment's chemical composition for the inhabited modules.

The main problem that arises with an increased duration of a space missions is that the currently available systems are unsuitable for such tasks. The disadvantages of hardware (architecture, ergonomics), software (inability to take into account the subtle properties of certain pollutants, for example, their polarity) necessitate the development and creation of qualitatively new subsystems included in the improved ILSS.

There is no single point of view regarding the issue of choosing the final configuration of the ILSS when preparing space missions. This potential solution for solving said problem is a creation of a dynamic simulation model which computes behavior of sources and sinks of trace contaminants that can be found in gaseous environment of an interplanetary manned spacecraft.

The paper illustrates:

1. Structure of the suggested simulation model
2. Mathematical depiction behind each sub-element of the model
3. Implementation in the LabVIEW software environment
4. Test results with the series of different scenarios and comparisons to actual data, gathered from ISS telemetry

Proposed simulation model tries to mitigate difficulties during the design phase.

It:

1. Simulates work process and calculates cooperation of different subsystems which functioning is based on following principles

– physical adsorption on solid sorbents (coals, silica gels, zeolites);
– heterogeneous catalysis, in particular catalytic oxidation (low/high temperature);
– condensation and solubility of trace contaminants in spacecraft's air moisture

2. Simulates and calculates mass balance for trace contaminants based on major sources such as crew's vital activities and non-metal materials' emissions;

3. Simulates the effects on gaseous environment of: transport/cargo spacecraft docking, extravehicular activities and commonly considered emergencies.

4. Considers the arrangement of systems in the ISS modules in order to identify the existence and calculate the expected degree of overlapping in order to determine the effective operating mode for profile equipment.

Several features are yet to be implemented:

1. Inclusion in overall simulation additional systems which function using chemisorption in liquid sorbents and photocatalytic oxidation;

2. More in-depth modeling of chemical and physical interaction between trace contaminants in the gaseous environment and during operational process of the air revitalization equipment;

3. Creation of an expansive library for types, parameters, quantitative/mass characteristics of trace contaminants with correlation to corresponding profile and non-profile systems.

FEATURES OF COMMUNICATION OF ISOLATED CREW OF MIXED NATIONAL AND GENDER COMPOSITION WITH THE CONTROL CENTER

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The purpose of our study was to clarify the communication tendencies of an autonomous crew, as well as to study the gender factor influence on the external communication of the members of an isolated small group.

The study of the crew - Mission control center (MCC) communication was executed within the Protocol of the 4-month isolation experiment SIRIUS-19, that was simulating some factors of the flight of the international mixed gender crew (3 men and 3 women, age from 29 to 45) to the Moon. A 5-minute delay in the crew-MCC communication was implemented. The main source of data for the communication analysis were video- and audio-recordings of the crew-MCC daily planning conferences. More than 20 categories of speech content analysis (such as «problem», «demand / request», «time perception»), and a number of categories representing stress coping strategies in the crew's communicative behavior («confrontation», «planning», «taking responsibility», etc) were utilized. The video recordings were also processed using FaceReader software in order to detect manifestations of basic emotions in the crewmembers' facial expressions. Speech acoustic characteristics reflecting the speaker's psychophysiological tension were analyzed using Praat software.

The influence of the gender factor on the style features of the crewmembers' communication was revealed using the content analysis method. In particular, statistically significant differences were found in the number of crew's statements attributed to the category «problem» and coping strategy «acceptance of responsibility / submission». This may indicate diversity in the communication styles of men and women in assessing and overcoming problem situations. Gender differences were also found

in the dynamics of the speech acoustic characteristics. In particular, the fundamental frequency of speech and the number of pauses decreased more in men than in women, while in women, the speech volume decreased more significantly. The difference between the speech characteristics recorded in the presumably stressful periods of isolation (including the acute period of adaptation and «landing» period) and in «normal» (stable) experimental conditions was less pronounced in women than in men. The results of the facial expression analysis also showed differences between gender subgroups. In particular, in the subgroup of women, there were more manifestations of both joy and sadness. In 2 participants (both male), there was a tendency for a decrease in the proportion of neutral facial expression during the experiment, while in 2 others (female), on the contrary, an increase in this indicator was observed.

In general, throughout isolation the communication styles of gender subgroups became more similar, with decreasing content variability and emotionality of speech. This tendency became especially pronounced in the second half of the isolation, after the period of landing simulation.

The study was supported by the Ministry of Science and Higher Education of the Russian Federation under the agreement No. _075-1502020-919 from 16.11.2020 about the grant in the form of subsidy from the federal budget to provide government support for the creation and development of a worldclass research center «Pavlov Center for Integrative Physiology to Medicine, High-tech Healthcare and Stress Tolerance Technologies».

MOTIVES FOR THE USE «IDEAL ANESTHETIC» XENON BE HUMANS IN SPACE

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The medical subtleties of a short stay in space, from a day to several months of practically healthy and specially trained people, differ significantly from the aspects of longer expeditions and interplanetary flights require significantly more time, require more detailed study of issues and solutions to various psychological problems, adaptation, compatibility. The implementation of a number of more complex, long-term projects is possible only with the provision of «gypobiosis», «artificial hibernation», «artificial hypothermia» that is in conditions that fall within the competence of the specialty anesthesiology-resuscitation. There may be cases when astronauts will need immediate surgery, there is a high risk of injuries when exiting and entering the space station from outer space, overloads on the entire musculoskeletal system of the body during takeoff to the space station landing. The observed acceleration of progress dictus the need to work in the mode of advance in anesthesiology similar term entered as preventive analgesia, with possibility of transition from 2030 years on the yse of environmentally friendly anesthetics, which intertwined with the planning interplanetary mission, start in 2030, which requires in-depth consideration of the issues of medical, and anesthetic management of crews n proactive developments in this direction. It is surprising that the evolution of anesthesiology and its methods since the last century has unconsciously developed in the direction of solving the problems of ecology, endoecology and cosmology. Anesthesiology and its methods have unconsciously developed in the direction of solving the problems of ecology, endoecology and cosmology. In the last century, the attention of chemists and anesthesiology was attracted by the inert gas xenon. With time, more recent studies of xenon has allowed to realize the possibility of using his e clinical anesthetic practice in the treatment of stress disorders of homeostasis of the human body, as well as a produce current, accelerating the flow of the night working fluid, which is supposed to use the inert gas xenon, for the expense of which creates the thrust, including medicines on the basis of xenon and the possibility of their recycling, meets the criteria accepted for aerospace equipment, high reliability, safety, low energy consumption, minimum mass, volume, recycling and could be used for biomedical ensure the long cosmology, for the solution of technical tasks, and medical tasks correction of psychosomatic disorders, correction of the symptoms of extreme fatigue, the application in order to provide analgesia and General anesthesia, the use of long-duration interplanetary and intergalactic expeditions (gypobiosis, artificial hibernation, hypothermia)

Conclusion. In our humble opinion, the possibility of science fiction, which, undoubtedly, despite the space goals, will give an impetus to the further development of medical technologies used in general clinical practice or Earth.

FIGHTING MICROBIAL BIOFILMS IN SPACE BY ESA'S UPCOMING SPACE MICROBIOLOGY AND MATERIAL SCIENCE EXPERIMENT BIOFILMS

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Long term human space missions require efficient strategies to sustain crew health and safety. This is why we need to develop improved spaceflight-suitable methods for microbiological monitoring and contamination control. Especially microbial biofilms are of concern in spaceflight because they can damage equipment by polymer deterioration, corrode metal and cause bio-fouling. Furthermore, biofilms can harbor pathogenic microorganisms that can cause infections which is unwanted, especially since it is known that the immune system of astronauts is impaired during spaceflight. Antimicrobial surfaces reduce the ability of microorganisms to form biofilms and can therefore be helpful in sustaining spaceship integrity as well as the astronaut's health. Metals such as silver, copper and their alloy are known to have antimicrobial properties. The introduction of antimicrobial surfaces for medical, pharmaceutical and industrial purposes has already shown a unique potential for reducing and preventing microbial contamination. However, their efficiency within the spaceflight context still has to be investigated in further detail:

The European Space Agency (ESA) selected project BIOFILMS (No. ILSRA-2014-054) will test the effect of tailor-made nanostructured copper-based surfaces on bacterial biofilm in an experiment aboard the International Space Station (ISS). BIOFILMS is an acronym that stands for «Biofilm Inhibition on Flight equipment and on board the ISS using microbiologically Lethal Metal Surfaces». In the project, three spaceflight relevant bacterial species will be tested: Acinetobacter radioresistens, Cupriavidus metallidurans and Staphylococcus capitis. Steel is going to be used as a refence surface for biofilm formation and the antimicrobial surfaces are copper-based. They differ in their antimicrobial activity based on chemical composition and/or geometric nanostructures. The innovative approach is that the surfaces are patterned in a process called Direct Laser Interference Patterning (DLIP) using ultra-short pulses (USP). The surfaces will be evaluated for biofilm formation rates under different spaceflight relevant gravitational regimes (Mars, ISS and Earth control) and bacterial growth will occur under optimal biofilm-inducing conditions in the KUBIK incubator inside ESA's Columbus laboratory.

Preflight experiments, performed on ground (1g), showed that the BIOFILMS hardware is biocompatible and allows biofilm formation of all three bacterial species on the reference steel surfaces. The use of pure copper and brass surfaces inside the hardware significantly reduced bacterial growth and biofilm formation. In our preliminary experiments, the DLIP nanostructured copper surfaces were more effective than the smooth surfaces.

The obtained results from the BIOFILMS experiment will be of immense importance for understanding the influence of gravity on biofilm formation and on the effectivity of USP-DLIP antimicrobial copper surfaces. Furthermore, the evaluation of different antimicrobial materials in microgravity is relevant for present and future astronaut-/robotic-associated activities in space exploration. Here, an overview on the ongoing and upcoming activities of the ISS spaceflight experiment BIOFILMS is presented.

EXPERIMENTAL ESTIMATION OF THE EFFECTIVENESS OF PROSPECTIVE METHODS OF PROTECTION OF THE HEARING ORGAN UNDER CONDITIONS OF HARMFUL EXPOSURE TO NOISE

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An experimental comparative assessment of the effectiveness of promising methods of hearing protection under conditions of exposure to «white» noise with an intensity of 85 dB and a duration of 2 hours in acoustically healthy volunteers was carried out. The results of the study indicate the presence of a positive effect when using inhalations of a normoxic oxygen-argon gas mixture.

Purpose of the study: to experimentally evaluate the effectiveness of promising methods of hearing protection under conditions of 2 hours exposure to continuous «white» noise with an intensity of 85 dB per person.

Materials and methods. The study involved 10 acoustically healthy male volunteers (26–43 years old), admitted by a medical expert commission to experimental studies with human participation. Exposure to «white» noise with an intensity of 85 dB and a duration of 2 hours was chosen as an acting factor, since it occupies the entire range of frequencies perceived by the human ear with the same amplitude and spectral density and makes it possible to achieve a time shift in hearing thresholds (TTS). Betahistine dihydrochloride and inhalation with normoxic oxygen-argon breathing mixture were used as promising methods for protecting the organ of hearing. For an objective assessment of the auditory system, the delayed otoacoustic emission (TEOAE) was recorded using the Neuro-Audio device (Neurosoft, RF). There were compared four series of the study: I – baseline studies of the state of the auditory system of the subjects; II - studies after exposure to noise («Noise-1»); III – studies after taking 32mg of betahistine dihydrochloride and subsequent exposure to noise («Noise-2»); IV – studies after a session of breathing normoxic oxygen-argon mixture and subsequent exposure to noise («Noise-3»). Statistical processing of the obtained results was carried out by the descriptive statistics method using the STATISTICA package. Comparison of parameter values included analysis of variance for Friedman's repeated observations. If statistically significant differences were found ($p \leq 0.05$), the mean values of the samples were compared using the Wilcoxon test.

Results. The signal-to-noise ratio in the frequency range of 1–4 kHz was statistically processed. Comparison of the signal-to-noise ratios of the background series of measurements and the «Noise-1» series revealed a significant decrease in the indicated indicators at a frequency of 4 kHz after exposure to noise for both right and left ears ($p = 0.005062$ and $p = 0.005673$, respectively). When comparing the signal-to-noise ratios of the background series and the «Noise-2» series, a significant decrease in these indicators at a frequency of 4 kHz was also revealed ($p = 0.056013$ for the right ears and $p = 0.028403$ for the left ears). Signal-to-noise ratios of the «Noise-3» series remained at the background level for the right and left ears ($p = 0.721277$ and $p = 0.646463$, respectively).

Discussion. A significant decrease in the signal-to-noise ratio of TEOAE in the series of studies «Noise-1» and «Noise-2» at a frequency of 4 kHz was associated with the occurrence of TTS observed in all participates. The use of betahistine dihydrochloride at a dose of 32mg did not demonstrate effectiveness in protecting the organ of hearing after a 2 hours exposure to «white» noise with an intensity of 85dB. The absence of negative dynamics of the signal-to-noise ratio in the «Noise-3» series demonstrates the otoprotective properties of breathing with a normoxic oxygen-argon gas mixture. The data of dynamic registration of noise levels in the astronaut habitat on the ISS indicate a trend towards exceeding the standard noise levels (Kutina I.V. et al., 2017). Despite measures aimed at reducing the acoustic pollution, a number of austroauts do not exclude the possibility of a damaging effect of continuous noise on the auditory system. The results of the investigation indicate the need for further study of the use of gas mixtures containing inert gases as promising means of protecting the hearing organ from the damaging effects of noise in long-term space flights.

THE NOVEL EXTRAPLANETARY RADIATION COUNTERMEASURES INITIATIVE (NERCI)

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The Space Radiation Element (part of NASA's Human Research Program) has recently initiated a multi-phase endeavor to identify biological countermeasures that can mitigate adverse long term health consequences of chronic low-dose-rate space radiation exposure, specifically carcinogenesis, cardiovascular and degenerative disease, and central nervous system dysfunction. To launch the Novel Extraplanetary Radiation Countermeasures Initiative (NERCI) the Space Radiation Element brought together an interdisciplinary team of researchers from top US institutions to develop a comprehensive strategy for target identification, high-throughput compound screening, drug discovery, and translational model development. Participants took part in a workshop in February 2021 and are now generating proposals to compete for NERCI «center» status. This presentation will highlight the results of that workshop and detail the strategy for NERCI moving forward.

PHASES OF ADAPTATION TO THE CONDITIONS OF «DRY» IMMERSION ACCORDING TO THE NEUROFUNCTIONAL STATE OF VOLUNTEERS

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Introduction. Changes in the functions of the central nervous system (CNS) of astronauts in space flight are observed. This is a central problem of space neurobiology for future long-term space missions. «Dry» immersion (DI) is a ground - based model of microgravity.

The aim of the work was a comprehensive study of the functional state of the CNS of volunteers for 5-day and 21-day DI and the stages of adaptation to the conditions of simulated microgravity.

Method. Dynamics of the CNS neurophysiological processes in 12 male during the 5-day DI and in 10 male during the 21-day DI study was tracked by way of plural brain investigations and tests including the concurrent EEG recording, measurements of the permanent potential levels (PPL). The presence of interhemispheric asymmetry and the degree of its severity; the dynamics of the averaged value over all leads and its spread (ΔPPL, mV) in the range (-100; +100 mV) were estimated from the values of PPL. In the EEG analysis, the dynamics of cortical activity indicators in the range of basic frequencies were studied, the type of pattern was determined, the relative power value (RP) in % and the value of the dominant frequency were estimated. The measurements were preceded by the simple reaction time test (SRT) and the Luscher test. Studies were performed at 5-day DI before and after the experiment. In 21-day DI before and on 7, 14, 21 days.

Results. After 5-day DI, stable adaptation was observed in 4 subjects. In 5 subjects CNS was transiting to a new level of adaptation; three were in the period of acute adaptation identified by abnormal anxiety, elevated PPL, decline of the α-activity and growth of total RP in the θ- and β1-bands. The adapted subjects were distinguished by lower or unaffected anxiety, RP growth in the α-band, and reduction or increase PPL no more than 2 mV. In 21-day DI on day-7, a buildup of the CNS tension was evidenced by growth of the EEG β1 relative power and PPL values. On day-14, the majority of the volunteers had been adapted to DI demonstrating prevalence of EEG pattern type-I and decreased PPL values. On day-21, data of the investigations reflected CNS excitation due to upcoming end of the study. Initial levels of anxiety varied from low to mean. On DI days 14 and 21, mean anxiety rose to the high level; based on SRT, the CNS state in volunteers with mean anxiety showed instability in different DI periods. Volunteers with the initially low anxiety remained unworried in the course of immersion which was favorable to their mental performance.

Conclusions. The comprehensive study showed that adaptation occurs on day 5 in 33 % of volunteers. On the 7th day, the intensity of processes in the CNS continues to increase. On day-14, the majority of the volunteers had been adapted to DI. Baseline neurophysiological investigations help detect people with unstable CNS conditions that may impact mental performance and, therefore, can be useful in selection of candidates for long-duration space missions.

GROUND LABORATORY STUDIES OF RADIATION EFFECT OF SPACE RAYS IN INTERPLANETARY SPACE

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In the study of interplanetary space on spacecraft (SC), there are risks of exposure of personnel and equipment of the spacecraft by cosmic rays (CR) and secondary radiation from the interaction of high-energy protons and heavy ions with elements of spacecraft structures. Relativistic CR particles create intense bremsstrahlung radiation and large local concentrations of evaporative neutrons, which can create a high dose of radiation to personnel and damage the material of structural elements. Radiation effects in space conditions differ significantly in their biological effectiveness due to the complex composition of radiation with an energy spectrum from several keV to hundreds of GeV. The CR component generating secondary neutrons with high multiplicity ($\sim 10^3$ in a time of ~ 3 ms) has a power-law energy spectrum with an exponent of -3.

The aim of the work was to assess the radiation risk of personnel overexposure and the harmful effects on spacecraft structural elements from GCR in interplanetary space in ground-based laboratory experiments and theoretical modeling.

The rigid CR component creates a high probability of the development of electron-photon cascades, an additional dose load from the radionuclides formed during activation.

At the high-mountain range of the Pamir-Chakaltaya International Research Center (4370 m above sea level, Tajikistan). measurements of background neutron fluxes were carried out on an X-ray emulsion chamber (REC) of the Lebedev Physical Institute. With the help of PDA-Pack Eya and MKC-PM140K radiometers, we investigated the multiplicity of fast neutron generation in the chamber materials under the action of the rigid CR component. The maximum neutron counting rate with the PDA-Pack Eya radiometer was 26 pulses / s. The neutron flux density measured with MKC-PM140K was 0.35 neutron / ($s \cdot cm^2$), which is 7 times higher than the level of the neutron background in the polygon sea level (Dushanbe).

Measurement of the intensity of scattered protons after interaction of a pulsed proton beam of a linear accelerator at an energy of ≥ 200 MeV. The dose of a proton beam pulse (10^6 p) absorbed by biological cells, measured using a Gafchromic EBT2 radiochromic film, was 1.2 mGy of local irradiation at the Bragg peak. In this case, the dose of the general radiation of the personnel from the part of the beam pulse scattered by the target (0.5 mm CH_2) was 0.25 mGy. The equivalent dose of fast neutrons from the interaction of protons with a biological sample, measured by the BDN-02R fast neutron detector, was about 1 mSv.

Radionuclides C^{11}, N^{13}, O^{14}, O^{15}, Ar^{41} with gamma radiation energies from 511 keV to 3 MeV can provide additional radiation load on the spacecraft crew.

BIOMEDICAL SUPPORT OF MANNED SPACE MISSIONS BEYOND THE LOW EARTH ORBIT AS AN ORGANIZATIONAL CONTROL SYSTEM

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The new stage of space exploration era will start with the humans' return to the Moon. The early unmanned and manned flights to the Moon in 1960s provided a wealth of information about the space environmental en route to the satellite. This information was shared with the biomedical community both in the USSR and USA. In this period researchers at the Institute of Biomedical Problems were tasked to define probable risks to living beings (humans) from spaceflight factors and to suggest methods and technologies that would ensure safety to crews during Moon exploration missions. However, for certain reasons the USSR space program underwent a revision that resulted in prioritization of constructing and operating long-term orbital stations. Renunciation of the Moon exploration program led to loss of the scientific interest in the Moon for decades.

To achieve the goal of landing cosmonauts on the Moon by the end of this decade, we will need to build an organizational system which will be in control of all the aspects of crew health, safety and functionality. The system will be charged with assessing the Technology Readiness Level (TRL) of every biomedical support element. The role of control instruments is to be played by the Biomedical certification council and Program management. These two bodies will consider progress level and endorse further activities. Input data for the system are lists of risks to crew health and biomedical technologies. Each risk and technology must be analyzed in order to determine an attainable TRL and to specify activities (roadmap) necessary to reach the next and/or the highest «flight readiness» level.

Integration of the activities included in a roadmap will be advantageous to optimal resources distribution. For example, ground-based isolation studies should combine a large variety of investigations and thus maximize the use of test subjects' time and minimize financial resources. This integration must not cause shifting of a roadmap implementation beyond 2030.

The Biomedical certification council will consist of experts in space medicine and physiology who will also supervise progress of a roadmap implementation. It may give an approval for shifts in the roadmap schedule if activities have been successful or require additional effort to verify results.

The Program management members are representatives of the Russian space institutions. The council function is to review and give go-ahead or reject alterations in roadmaps proposed by the Biomedical certification council.

Means and methods designed to secure crew safety and functionality during missions to the Moon must be tested in ground-based experiments. Both efficiency and functionality must be presented to the Biomedical certification council with participation of space payload and vehicle specialists. The Council conclusion may have a statement to the effect that the presented technology is ready for flight testing onboard the orbital station. Results of the flight testing are to be reported to the Biomedical certification council and Program management as evidence that means and method under consideration is ready for integration into Moon exploration vehicles. The roadmap will be then closed as complete.

Development of this organizational system will allow also to use this instrument in preparation for further manned space missions, including deep space exploration.

RADI-N2 AND MATROSHKA-R: MEASUREMENTS OF NEUTRON RADIATION ON THE INTERNATIONAL SPACE STATION (2009–2020)

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Protection of crewmembers from radiation is a high priority for long-duration spaceflight, including exploration missions to the Moon and Mars. Radiation in deep space is a mixed field due to galactic cosmic rays (GCRs) and solar particle events. In low-Earth orbit (LEO), protons and electrons trapped in the Van Allen belts also contribute to the radiation field. Neutrons encountered in LEO, for example on the International Space Station (ISS), are produced predominantly by nuclear interactions of GCRs and trapped protons with various elements in the walls and interior components of the spacecraft, and by neutron albedo from GCRs incident on the Earth's atmosphere. Previous studies in LEO have shown that neutrons contribute significantly to the radiation dose received by the crew. A significant contribution from secondary neutrons is also expected for deep space missions.

The primary goal of Radi-N2 is to characterize the neutron dose equivalent and energy distribution in multiple locations in the US Orbital Segment (USOS) of the ISS over an extended period of time. The measurements used multiple bubble detectors, which are passive neutron dosimeters based on superheated liquid droplets dispersed in a polymer gel. Bubbles in the detectors were counted using an automatic bubble reader located in the Russian Orbital Segment (ROS). The preceding Radi-N experiments were conducted in 2009 in three USOS locations: Columbus, the Japanese Experiment Module, and the US Laboratory. The Radi-N2 measurements began in 2012 in these three ISS modules, later extending to include Node 1, Node 2, Node 3, and the Cupola. By the conclusion of the measurements in 2020, 75 week-long sessions (including three sessions for Radi-N) had been conducted in the seven USOS locations. The Radi-N2 data enable an assessment of the effects of solar activity on the neutron field in the ISS over the period 2009 – 2020, which corresponds to a full solar cycle. The influence of other quantities, including the ISS altitude and location within the ISS, is also under investigation. For some sessions, one bubble detector was worn by a Canadian astronaut, while a second detector was located in their sleeping quarters. These data provide a comparison of the neutron dose equivalent in the sleeping quarters to that accumulated during daily activities around the space station.

Radi-N2 is conducted within the framework of the Matroshka-R experiment. As part of the work, experiments were conducted using bubble detectors in the ROS, concurrently with the USOS surveys. Measurements in the ROS assessed the neutron field in multiple locations: the Zvezda Service Module, the Pirs Docking Module, the Rassvet (Mini Research Module 1), the Poisk (Mini Research Module 2), and the Zarya Functional and Cargo Module. A number of experiments were conducted in the ROS using a tissue-equivalent phantom and a hydrogenous water shield. Data from these measurements enable an evaluation of the absorption and production of secondary neutrons in the human body and the efficacy of reducing the neutron dose equivalent using water-based shielding.

This paper is dedicated to the memory of our friend and colleague Sergey Khulapko.

ON THE POSSIBILITY OF USING GVS-TECHNOLOGY FOR VISUAL FLIGHT CONTROL IN EXTREME SITUATIONS

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The report is devoted to the presentation of a possible research plan «Application of the technology of galvanic vestibular stimulation in extreme conditions of professional activity of astronauts during the installation of large structures in orbit and research activities on the lunar surface». The report, consisting of 3 parts, will present:

– substantiation of the possibility of galvanic correction of the activity of vestibular mechanoreceptors within the framework of the created mathematical model based on the results of experiments in 2001–2011;

– implementation of the experiment on a flight-dynamic stand with 6 degrees of freedom «Galvanic vestibular stimulation with a coordinated turn» in 2016–2018;

– description of the 3 stages of the space experiment on board of the ISS in 2017–2027.

The report is dedicated to the memory of academician I.B. Kozlovskaya.

The work is supported by Funding CONACyT, AEM - Agencia Espacial Mexicana (Mexico) and Roscosmos.

BRAIN CHANGES IN RESPONSE TO A COMBINED EXERCISE AND SENSORY STIMULATION COUNTERMEASURE DURING LONG-DURATION ANTARCTIC MISSIONS

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Reduced sensory stimulation and sensory monotony experienced in isolated, confined, and extreme (ICE) environments are thought to contribute to the potential development of adverse behavioral conditions and/or psychiatric disorders. We previously reported that prolonged isolation and confinement associated with overwintering in Antarctica induce significant

brain changes that are associated with reductions in brain-derived neurotrophic factor (BDNF). Here we investigated whether previously reported brain changes and reductions in key neurotrophins could be mitigated by a countermeasure combining physical exercise with an interactive virtual environment which we termed Hybrid Training (HT). Data were collected across two separate winter-over missions. Each Neumayer III mission comprised a total N = 9 crewmembers who were invited to take part in the experiment, yielding a total of N = 16 (5 women) for the HT sample. Crewmembers were encouraged to perform HT at a moderate intensity three to five times per week. Data were compared to N = 17 (6 women) Neumayer III crewmembers from previous winter-overs who did not have access to HT (CTRL). Neuroimaging was performed about 1.5 months before and after completion of the expedition. Venous serum blood and saliva samples were collected 1.5 months before, after 3 months, 7 months, and 11 months in-mission, and 1.5 months after the expedition. All samples were taken in the morning after an overnight fast, and preprocessed following standard procedures. BDNF, vascular endothelial growth factor (VEGF), insulin-like growth factor 1 (IGF-1), and 25-Hydroxy-Vitamin-D (Vit D) were assessed in duplicate using enzyme-linked immunosorbant assays. Cortisol concentrations were quantified in saliva samples using electrochemiluminescence immunoassays.

On average, each crewmember performed an average of 81HT sessions (95 % CI: 33, 129). Notably, these data were characterized by considerable inter-individual variability in HT frequency with one crewmember completing 271 HT sessions, and another one performing a single familiarization session. The mean exercise intensity was approximately 72 % HRmax (95 % CI: 69, 75), corresponding to light/moderate aerobic exercise. To examine the impact of HT on BDNF, IGF-1, VEGF, Vit D, and Cortisol we compared the data across the mission between HT and CTRL. We found significantly higher serum BDNF, VEGF, and Vit D levels in HT compared to CTRL. The interaction between time and group on hippocampal subfields did not reach statistical significance. However, a comparison of change scores between HT and CTRL revealed some considerable effect sizes (Cohen's d = 0.6 and 0.9 for dentate gyrus and CA1), characterized by smaller hippocampal subfield reductions in HT compared to CTRL. We also observed widespread decreases in gray matter across the whole brain (including the right medial prefrontal cortex, precuneus and supramarginal gyrus, parahippocampal cortex and lingual gyrus, calcarine cortex, and posterior cingulate cortex) in CTRL relative to HT. In conclusion, our data suggest beneficial effects on mitigating brain changes and upregulating key neurotrophins during prolonged isolation and confinement.

Future work needs to assess the phenotypic differences in response to the training, account for factors other than training characteristics, and identify whether the increases in biomarkers are also associated with behavioral manifestations.

This study was supported by NASA through grant NNX16AI53G and DLR through grants 50WB1525 and 50WB1330.

ALTERED GRAVITY CONDITIONS IMPAIR SPATIAL COGNITION

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Spatial navigation is an important cognitive ability for maintaining operational performance in complex procedures such as docking or landing tasks, and exploring unknown planetary terrains. On Earth, this ability critically depends on the integration of visual, proprioceptive, kinesthetic, and vestibular information. Weightlessness significantly reduces the amount of information forwarded by the vestibular system. Accordingly, cosmonauts and astronauts have experienced vestibular disorders during the transition to weightlessness, including spatial illusions, disorientation, vertigo, and motion sickness. Despite its vulnerability and importance for long-duration exploratory space missions (LDEM), research on spatial navigation has only received little attention. In preparation of the ESA/DLR ISS experiment HypoCampus and NASA's CIPHER experiment Spatial Cognition we designed a specific assessment tool to monitor visuo-spatial abilities during long-duration spaceflight. A unique feature of this tool is that it allows for the assessment of distinct abilities that are critical for spatial navigation.

The aim of the present study was to assess the sensivity of one of the battery's task during changing gravity conditions. We hypothesized that orientation would be impaired in response to altered gravity during parabolic flight maneuvers. Maintaining orientation requires spatial updating, the continuous monitoring of self-motion cues to update external locations. As part of an ESA parabolic flight campaign 10 healthy subjects (4 women, 6 men), aged 33 to 50 years, performed a visual spatial updating task comprising two updating conditions simulating virtual forward movements of different lengths (short and long), and a static condition with no movement that served as a control condition. Two trials were performed during each phase of the

parabola, i.e., at 1 g before the start of the parabola, at 1.8 g during the acceleration phase of the parabola, and during 0 g. Our data demonstrate that 0 g and 1.8 g impaired pointing performance for long updating trials as indicated by increased variability of pointing errors compared to 1 g. In contrast, we found no support for any changes for short updating and static conditions, suggesting that a certain degree of task complexity is required to affect pointing errors. These findings are important for operational requirements during spaceflight because spatial updating is pivotal for navigation when vision is poor or unreliable and objects go out of sight, for example during extravehicular activities in space or the exploration of unfamiliar environments. Future studies should compare the effects on spatial updating during seated and free-floating conditions, and determine at which g-threshold decrements in spatial updating performance emerge.

This study was supported by the European Space Agency (ESA) and the German Aerospace Center (Deutsches Zentrum fьr Luft- und Raumfahrt; DLR) through grants 50WB1525 and 50WB1915.

THE GERMAN SPACE LIFE SCIENCE PROGRAM: BENEFIT FOR PEOPLE ON EARTH

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The German Space Life Sciences Program is managed by the German Aerospace Center (DLR) in its role as National Space Agency and located within the department of Research and Exploration.

The program focuses on exploring nature (Gravitational, Radiation and Astro-Biology), improving health (Integrative Physiology, Diagnosis and Therapy, Telemedicine) and enabling exploration (Biological Life Support Systems, Health and Performance of Astronauts). The overall goal is to gain scientific knowledge and disclose new application potentials by research under space conditions, especially by utilizing microgravity platforms such as the International Space Station. For implementing the program, DLR provides not only both infrastructure and access to flight opportunities such as drop tower, sounding rockets and parabolic airplane flights, but also funds science teams from German universities or other research institutes and gives out contracts to German industry for hardware development. The International Space Station ISS is utilized via Germany's participation in the ESA Microgravity Science Program and via bilateral cooperation with other space agencies, free flyers are used via cooperation with agencies around the world.

The talk will focus on the department´s engagement in current Space Life Science projects and give an overview on major German research topics and on-going facility developments for the ISS and other microgravity platforms. Some examples for human physiology research will be highlighted. ISS research is accompanied by the utilization of other flight opportunities, as all space research is embedded in and complemented by terrestrial research, e.g. by simulation, isolation and bedrest studies. With this broad approach, the transfer of the gained knowledge and technologies to benefit the people on earth is strengthened and maintained. The status of future perspectives for the German Life Science.

Program will be prospected, involving chances opened up by new platforms and «new space 2 working structures, in which the important role of international cooperations constitutes – more than ever – the basis for success.

NASA UPDATE ON SPACEFLIGHT ASSOCIATED NEURO-OCULAR SYNDROME: RECENT FINDINGS AND FUTURE PLANS

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Spaceflight Associated Neuro-ocular Syndrome (SANS) is characterized by ocular structural and functional changes, including hyperopic shifts, optic disc edema and chorioretinal folds, and may also be influenced by structural changes to the optic nerve and brain. Recent International Space Station (ISS) studies such as Ocular Health and Fluid Shifts have helped to refine our understanding of the time course and recovery of SANS findings, including novel discoveries of increased lateral ventricle volumes and venous flow stasis that might be contributory mechanisms. Furthermore, SANS findings were recently reported in a strict head-down tilt analog, with and without ISS-like CO2 levels, providing an analog in which to test mechanisms and countermeasures. The purpose of this presentation is to summarize recent flight and analog SANS findings, and to discuss future directions for understanding and mitigating this risk of long duration spaceflight.

EYE EXAMINATIONS IN BED REST STUDIES TO MAINTAIN OCULAR HEALTH AND TO DEFINE SUCCESSFUL APPLICATION OF COUNTERMEASURES

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Introduction. Long-duration space travel challenges ocular health as evidenced by the «Spaceflight associated Neuro-ocular Syndrome» (SANS). The syndrome comprises optic disc edema, choroidal folds, cotton wool spots, globe flattening with hyperopic shift, and enlargement of the optic nerve sheath distension. In the VaPER study, 30 days strict -6° head down tilt with raised ambient CO2 and without pillows reproduced SANS-like findings in 5 of 11 subjects. Subsequently during the following 60 day, -6° head down tilt AGBRESA study with a normal atmosphere, 11 of 24 test subjects developed optic disc edema.

In the past, International Standard Measures during bed rest studies included ocular ultrasound, tonometry, and fundus examination, which was replaced by Optical Coherence Tomography (OCT), to monitor potential changes in test subjects and make their participation as safe as possible. However, more detailed examinations may be required.

Examinations. To identify acute eye diseases and to monitor potential changes in ocular health, we perform tests both, before and after the bed rest phase, as we also do in astronauts before, during and after the spaceflight mission. Testing includes best corrected visual acuity in distance and near, visual field testing, slit lamp examination, tonometry, color vision, ultrasound, objective refraction and fundoscopy with fundus imaging in cycloplegia, Heidelberg Retina Tomography (HRT), and OCT. Objective refraction in cycloplegia can detect hyperopic shift, visual field exams can detect retinal and optic nerve changes, and color vision exams can detect changes in optic disc diseases. HRT gauges the optic nerve head and OCT quantifies optic nerve and retinal thickness with high sensitivity. Being the first one worldwide to perform OCT during the head down tilt phase of bed rest we could demonstrate, that the OCT star pattern identifies changes better than the formerly used circle scan. During the bed rest phase, we perform near visual acuity to identify early hyperopic shifts with a decrease in near visual acuity and tonometry because intraocular pressure rises, especially during the first phase of bed rest. In case of a relevant increase in retinal thickness, we individually also perform direct ophthalmoscopy to exclude optic disc edema. Optic disc edema can only be diagnosed by fundoscopy which we performed in bed rest studies. In the AGBRESA study, we introduced visual field testing and objective refraction, as well as subjective refraction measurements in the supine position for the first time during a bed rest study.

Conclusion. Recognition of SANS-like findings during head down tilt bed rest provides an impetus for more detailed ophthalmology examinations. In addition to maintaining ocular health of participants in bed rest studies, more detailed testing should be required by the space agencies (especially fundoscopy and OCT) during the bed rest phase, but also months to years after to ensure test subject safety and progress in SANS mechanisms and targets for countermeasures.

CELL RESPIRATION OF SPERMATOZOA OF THE FRUIT FLY *DROSOPHILA MELANOGASTER* UNDER SIMULATED MICROGRAVITY

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The deep space exploration by human in the future will face the problem of maintaining the viability of the species, which indicates the need to answer the question about the role of gravity in the development of organisms.

The aim of this study was to determine an effect of simulated microgravity for 1, 3, and 6 hours on cell respiration, sperm motility of the fruit fly *Drosophila melanogaster*, as well as on the content of cytoskeletal proteins. Cell respiration was determined by polarography, sperm motility was determined using video recording and analysis of the resulting video files, and protein content was determined by western blotting. All procedures conducted with animals were approved by the Commission on Biomedical Ethics of the Institute of Biomedical Problems (IBMP), the State Scientific Center of the Russian Federation (Minutes No. 521 dated 25 September 2019).

The rate of oxygen uptake by permeabilized testes (basal), the rate of oxygen uptake with the addition of exogenous substrates (glutamate + malate), the maximum rate with the addition of the saturating concentration of ADP, and the respiratory rate after inhibition of the first and third complexes of the respiratory chain did not differ from the corresponding levels in the control group.

When measuring sperm motility after exposure to simulated microgravity for 1 and 3 hours, no changes were observed compared to the control group. After 6 hours exposure the rate increased by 34 % ($p < 0.05$) compared with the control

group, amounting to 58.5 ± 2.6 μm/s, and the beat frequency decreased by 33 % ($p < 0.05$), amounting to 0.93 ± 0.09 Hz, respectively.

The content of cytoskeletal proteins, specifically alpha-tubulin, beta-tubulin, subunit 4 of the Tcp1 complex, which form the sperm tail axoneme, did not change relative to the control group.

Based on the above, simulated microgravity increases the motility of the sperm tails of the fruit fly *Drosophila melanogaster*, while the absence of changes in the protein pattern and cell respiration suggests that the change in rate may be associated with the regulation of phosphorylation of motor proteins, which requires further study.

This work was financially supported by the program for fundamental research SSC RF – IBMP RAS 65.4 and Strategic Academic Leadership Program.

SPACE POLICY, MANAGEMENT SYSTEMS, PUBLIC SECTOR

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This paper includes a follow-up development of the research in space-based management systems (Sb-sms), which was incubated in the focus topic of space policy and for the public sector dissemination. Amongst the agenda highlighted is the sustainable space economy, and inclusion of astrobiology role supporting new frontier dimensions concerning the programming for Sb-sms. The modelling of Sb-sms though remains amateur in its functions, the current modelling enables data analysts and policy makers to investigate the reality of sustainable outer-space questions which may be lacking (hitherto) in the past decades of bibliographic source for space policy. A circular data management system, different from geographic modelling methods is debated for the development of Sb-sms, while at the same time the imparted usefulness of studying subjective knowledge regarding sustainable space policy provides more inward results that is more interpretable for public sectors readers.

PHARMACOLOGICAL INDUCTION OF HYPOBIOSIS: TRENDS AND PROSPECTS. PART II. LONG-TERM PHARMACOLOGICAL TORPOR WITH FEEDBACK-CONTROLLED DRUG ADMINISTRATION

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Pharmacological hypothermia and torpor can be used to protect astronauts during long space missions. Earlier, we have developed a pharmacological composition (PC) that initiates a pharmacological torpor (PT), made up of eight therapeutic agents, inert gas xenon and lipid emulsion served as a drug vehicle. In the presented work, we have proposed an automatic system to maintain a multi-day PT using multiple small-dose injections of PC and a nutritional compound with computer-controlled feedback. Two computer-controlled automatic syringe pumps were used for the intravenous injection of PC and nutrition. To monitor body temperature, we used an implanted compact sensor. The collected data were transmitted to a computer for analysis and control of the syringe pump operation.

To initiate hypothermia the initial bolus injection of PC was applied. Then, to maintain hypothermia, numerous small-dose injections of PC were performed in the moments when the body temperature of the animal reached the threshold value that we set at 33 °C. After stopping the supply of PC, the hypothermia persists for several days, after which the normal body temperature was spontaneously restored. Immediately after that, the motility of animals was low, however, on the next day the animals willingly consumed water and food, and after a week their behavior was fully restored.

Our proposed approach to initiating PT with automatically controlled multiple injections of small doses of PC and nutrients has a prospect of application in medicine and astronautics.

QUANTITATIVE APPROACH TOWARDS AN ANALYSIS OF STRUCTURE AND DYNAMICS OF SOCIAL RELATIONSHIPS IN SPACE CREWS

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Goals. Contribution sets as its goal to introduce possible quantitative data analysis methods in the area of social relationships. Relationships among the crew members directly affect work performance as well as resilience and psychological health of the crew members. Detecting the changes in structure and dynamics of these relations (one-time significant changes and also lon-term, harder to detect, terms) and early-following preventive and intervention measures can prevent and eliminate many risky phenomenons such as, for instance: dividing the crew into more sub-groups, isolation of a crew member, presence of serious conflicts among the crew members or between the crew and the mission control center.

Method. Possible ways in quantitative data analysis of relationships and their advantages and limits are introduced, based on the results of isolation experiments SIRIUS 17 a SIRIUS 18/19. The study focuses on the analysis of communication and cooperation, where relationships are manifested. As a follow-up to the social-action research methodology, the Sociomapping method was chosen as a primary research method. The method covers three subsequent levels: diagnostics, visualization, and intervention. The presentation illustrates the diagnostic part of the technique - analysis of communication and cooperation scales using control charts and correlation analyses between subsequent measures, etc.

Results. Final data analyses of the six-member crew, gender-heterogenous crews of experiments SIRIUS 17 and SIRIUS 18/19, through the above-described methods, show significant changes in dynamics and structure of relationships during conducted simulations. Based on these results, the advantages and limits of the particular statistical analyses are discussed, as well as the benefits of presented findings for other realized analog missions, and also real space flights.

EFFECTS OF CRANIAL PROTON IRRADIATION ON VISUOMOTOR BEHAVIOUR IN NONHUMAN PRIMATES

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The instrumental conditioning efficacy and latencies of visually guided saccades and manual reactions were studied in three monkeys (Macaca mulatta) following single cranial irradiation with high-energy protons (170 meV, 3 Gy). Such exposure simulates a radiation effects to humans during long-duration deep space missions.

The animals were trained to perform a visuomotor instrumental conditioning task. They performed saccades to stimuli presented in a wide visual field and responded to them manually by pressing a lever, thus modeling some of the basic components of human operator activity. Two animals demonstrated a monotonous decrease in motivation when instrumental conditioning performance during three months after irradiation (a.i.), although performance efficiency remained high. One monkey demonstrated a slight (in one month a.i.) and then dramatic (in next month) increase in latencies of saccadic and manual reactions, returning to the level of the first month a.i. in next two weeks. Another monkey demonstrated similar dynamics only in manual latencies. Control animal did not demonstrate any dynamics in neither saccadic nor manual latencies after sham irradiation. We also found that irradiation had different effects on latencies with regard to visual stimuli eccentricity. Saccades to the stimuli in the macular visual field were affected most of all.

One monkey underwent local irradiation of parietal cortex in Bragg peak. Three weeks a.i. the increase in manual latencies was revealed that persisting to up to 160 days. However, there was no decrease in motivation or performance efficiency in this monkey. We believe the effect of local irradiation in Bragg peak was higher due to greater intensity of radiation exposure. These results suggest that irradiation causes temporary decrease in motivation and coherence of integrative and executive processes underlying oculomotor and visuomotor performance.

As to the cognitive aspects, we used GAP and OVERLAP paradigms of visual stimulation to study visual attention shift, which is demonstrated as a difference in saccadic latencies in these paradigms. During the second month a.i. this parameter in one monkey increased gradually and then decreased, while in other monkey we noticed only slight increase over three months a.i. This means that irradiation affects dynamic characteristics of attention. The left and the right visual hemifields were affected differently, which is manifested in different saccadic and manual latencies performed in response to stimuli in the left or right hemifield. These latencies asymmetry assumes that proton irradiation may affect lateralization of different aspects of perception.

In addition, monkeys were trained to perform operant task, in which they had to grasp the food from an experimental box. This task was completely unaffected by proton irradiation in all three monkeys.

In general, our results demonstrate that systemic processes underlying instrumental and operant behaviour are relatively impervious to irradiation with high-energy protons. However, the exposure resulted in an increase of manual reactions latencies. In addition, the exposure also affected cognitive processes, namely attentional dynamics, perception lateralization and the spatial aspects of visuomotor performance.

Supported by the Russian Fund for Basic Research (grant No. 17-29-01027 ofi_m).

THE FIRST FEMALE DRY IMMERSION (NAIAD-2020): DESIGN AND SPECIFICS OF A 3-DAY STUDY

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The report presents the procedure and some results of the first study on the female Dry Immersion.

As the participation of women in space flight missions becomes more and more regular, it is of importance to study the women's health under the influence of space flight factors. In particular, previous studies have shown that women are more susceptible to orthostatic stress, space motion sickness and radiation. Despite the fact that gender differences should be taken into account during the preparation for long-term missions, this issue has not been fully studied, in particular, due to a small number of female cosmonauts/astronauts. Therefore, the attention of researchers is focused on the study of the functions of the female body not only in a real space flight, but also in model conditions.

Dry immersion (DI) is one of the most widely used ground-based models of microgravity. This model has been successfully used in men for over 50 years. However, the studies involving this model with the participation of women have not yet been conducted, in part, due to a number of hygienic and physiological difficulties.

The aim of this study was to perform a short-term 3-day immersion, as well as to analyze the tolerance of exposure and describe the medical risks in a group of women of reproductive age at these conditions.

The NAIAD-2020 experiment was conducted at the Institute of Biomedical Problems of the Russian Academy of Sciences with the participation of six female health volunteers of reproductive age (age: 30,17 ± 5,5 years; height: 1,66 ± 0,1 m; weight: 62,05 ± 8,4 kg). The start of immersion for all participants was at the 7th day of the menstrual cycle, and its completion - at the 10th day. The studies of the recovery period continued for another 7 days after the completion of the immersion exposure.

It is interesting to note that during DI, women did not show a significant increase in height, which may be due to the greater plasticity of the connective tissue. Women experienced discomfort in the lumbar region to a lesser extent compared to the male group, which requires further research. Also during DI women showed a more pronounced psychological discomfort during urination than in the group with the participation of men. However, it remains unclear whether the psychological discomfort was a cause or, on the contrary, a consequence of urination disorders. From the experience of space flights with the participation of women, it is known that in real weightlessness similar urination disorders are observed.

The results of the studies did not find significant risks to women's health and showed the feasibility of using this model of the effects of space flight with the participation of women of reproductive age.

The study is supported by the Russian Scientific Foundation (project #19-15-00435).

COGNITIVE SCIENCES OF COMMUNICATION AND ACTION

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Staying in environments subjected to states of hypo or microgravity produces specific processes of modification and reorganization of cognitive and motor functions in humans, referable to connectome remapping processes. The scientific data collected to date during manned missions have allowed the understanding of specific «psychophysiological evolutionary dynamics» that characterize the stay of crews in an extraterrestrial environment. The success of the missions, however, does not depend only on the specific technical or scientific skills of each crew member. In particular, when setting up long-stay missions, it appears necessary to compose the crews taking into account some often neglected overstandard parameters. With this lecture we intend to illustrate some theoretical parameters related to the most recent research in the field of cognitive sciences, developed through approaches that propose cognitive models according to multimodal processing protocols and multisensory information processing.

Starting from some peculiarities of the neural remapping produced in humans subjected to long stay in confinement conditions even in hypo and microgravity states, some useful data will be identified both for the future selection procedures and for the training of aspiring cosmonauts destined for long-term missions in deep space.

SLEEP ARCHITECTURE CHANGES DURING 21-DAY DRY IMMERSION

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Introduction. A decrease in sleep quality and quantity during space travel has been repeatedly reported (Polyakov et al., 1994; Gundel et al., 1997; Barger et al., 2014). However, the exact mechanisms that underlie this effect remain unclear. In space, sleep might be impacted by weightlessness and its consequences for cardiovascular, sensorimotor, and neurovestibular functions. The most appropriate ground-based model for the studies of hypogravity effects is dry immersion. In the present study, we aimed to explore the changes of night's sleep architecture during 21-day dry immersion.

Methods. Eight healthy male volunteers aged 20 to 40 years participated in the study. Objective sleep architecture evaluation was performed by overnight polysomnography (PSG) at baseline, at the 3rd, 10th, and 19th day of dry immersion, as well as after one recovery day. PSG recordings included an electroencephalogram, electrooculogram, electromyogram, electrocardiogram, airflow, thoracic and abdominal movements. PSGs were scored offline by two scorers who were blinded to the experimental conditions.

Results. On the 3rd day of immersion, PSG data showed dramatically disorganized sleep architecture: the number of awakenings has doubled, the duration of wake after sleep onset (WASO) increased four times compared with the baseline. Besides, the duration of rapid eye movement (REM) sleep and non-rapid eye movement (NREM) stage 2 significantly decreased. On the 10th day of immersion, there were signs of sleep recovery and the return of its architecture to baseline values. On the 19th day of immersion, the PSG characteristics were comparable to the baseline ones. However, REM sleep duration increased and became significantly longer than in the baseline and on the 10th day of immersion. After one recovery day, REM sleep duration returned to its initial values; the other architecture parameters also did not differ from the baseline.

Conclusion. The results suggest that the most pronounced sleep disturbances occur on 3rd day of dry immersion. The recovery of sleep architecture, observed on the 19th day, may reflect the adaptation of the organism to the abnormal environment. Further research is needed to understand the role of REM sleep increase in coping with hypogravity. Considering the neuroprotective properties of REM sleep (Pastukhov, Simonova, 2018) and its role in brain recovery during the acute phase of stroke (Pace et al., 2017), we can assume that the increase in REM sleep might be associated with cerebral plasticity underlying regulatory changes in a variety body system. In particular, with the reorganization of peripheral and central blood flow following the centralization of body fluids.

The study is supported by the Russian academy of sciences (Themes 63.1, 64.1).

THE EFFECTS OF SLEEP DISTURBANCES ON WORKING MEMORY ARE MEDIATED BY CHANGES IN MELATONIN LEVEL

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Introduction. Disrupted sleep is a common and important problem during space flights (Polyakov et al., 1994; Gundel et al., 1997; Barger et al., 2014). Insufficient sleep quantity and quality influence vigilance and cognitive functioning in astronauts (Petit et al., 2019). The exact neurophysiological underpinnings of these effects, however, remain unclear. Among the candidates are the changes in secretion of neuroactive hormones, particularly melatonin. The main function of melatonin is the circadian organization of physiological processes: in the evening, the rise in circulating melatonin prepares the body and brain for the sleep period, its decline in the morning adjusts physiological processes in anticipation of the intense daytime activity. As we have shown earlier, slow-wave sleep (SWS) suppression during one night's sleep leads to an increase in morning melatonin levels (Ukraintseva et al., 2020). Considering the neurocognitive effects of melatonin (Arendt et al., 1984), these changes may impair cognitive functions.

We used a model of selective SWS and rapid eye movement (REM) sleep suppression to compare the effects of SWS and REM disturbances on melatonin secretion and to explore the impact of elevated melatonin on working memory.

Methods. Twelve male volunteers participated in three experimental sessions: a session with SWS suppression, a session with REM suppression and a session with a regular night's sleep (control). Suppression was achieved by presenting an acoustic tone with a gradually rising sound intensity until the occurrence in polysomnogram signs of lighter sleep stages. Each session included collecting seven salivary samples: at 20:00, 21:30, 23:00, 01:30, 04:00, 07:00 (immediately after awakening) and at 07:40. After the first saliva sample was obtained and until bedtime (i.e. until 23:00), participants were kept in dim-light conditions. Night samples and the first morning sample were collected in the dark. The samples were analyzed by liquid chromatography-tandem mass spectrometry for melatonin. In the evening and in the morning, participants completed task on working memory (n-back).

Results. Preliminary results show that in the session with SWS suppression, SWS duration was reduced by 55 % compared with the control condition; in the session with REM suppression, REM was reduced by 52 %. Morning melatonin significantly increased after the night with SWS suppression compared to the control night, and its level was even higher after the night with REM suppression. Disturbed sleep was followed by a decrease in n-back score. In both sessions, with SWS and REM suppressions, working memory impairment was associated with an increase in morning melatonin.

Conclusion. The results suggest that disturbed sleep leads to increased melatonin secretion, and the effect of sleep disturbance on cognitive functions might be mediated via elevated melatonin. As poor sleep quality is a common problem during space missions, elevated melatonin as its consequence should be considered carefully.

This work was supported by the RFBR grant № 19-313-90067.

STRESS CAUSED BY PSYCHOLOGICAL AND PHYSIOLOGICAL STRESS SIGNIFICANTLY CHANGES THE CONCENTRATION OF CIRCULATING DNA IN HUMAN BLOOD PLASMA

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Introduction. Fragments of cell-free DNA (cfDNA) circulate in the blood plasma of a healthy person. One of the main cfDNA sources are dead body cells. CfDNA concentration determination allows assessing the level of cell death in the body under strong impacts (high radiation, psychological stress, physical loads stress and weightlessness). The aim of the present study is a comparative analysis of previously obtained and published data on cfDNA concentration in blood plasma in humans under various conditions.

Materials and methods. We analyzed previously published data on cfDNA concentration in samples: (1) healthy people (N = 597); (2) cosmonauts (before and/or after flight) and subjects who participated Mars-500 and Sirius programs at the peak load (N = 48); (3) employees of Rosatom State Corporation who for a long time worked in conditions of high radiation (N = 178); (4) patients with acute mental illnesses (N = 335); (5) patients with rheumatoid arthritis and systemic lupus erythematosus in the acute stage (N = 212) and (6) patients in the intensive care unit (N = 121) with various diseases (trauma, stroke, heart attack, sepsis). All cfDNA concentration tests were performed by employees of «Research Centre for Medical Genetics» using same method, including the cfDNA samples extraction from lysed plasma samples treated with RNAse and proteinase K, using organic solvents extraction and alcohols sedimentation. DNA concentration in isolated samples was determined fluorimetrically. Distributions and concentration values were compared using nonparametric Kolmogorov-Smirnov (D, α) and Mann-Whitney (p) statistics.

Results. CfDNA concentrations values were: (1) 268 ± 287 (median 152) ng/ml; (2) 1776 ± 1832 (median 1235) ng/ml; (3) 360 ± 622 (median 101) ng/ml; (4) 1554 ± 1703 (median 933) ng/ml; (5) 1509 ± 1671 (median 870) ng/ml; (6) 25591 ± 54420 (median 7100) ng/ml. CfDNA concentrations distributions for samples (2), (4) and (5) (cosmonauts and test subjects at peak loads, patients with psychosis and patients with exacerbation of autoimmune diseases) practically coincide with each other and significantly differ from the distributions (1) and (3) (control and Rosatom employees) by large values of cfDNA concentrations ($D = 0.63$ $\alpha < 10–20$; $p=0$). The distribution (6) for intensive care unit severe patients differs significantly from distributions (2), (4), and (5) by large cfDNA concentrations ($D = - 0.63$ $\alpha < 10–11$; $p<10\text{-}14$).

Discussion and conclusions. In flight conditions and simulation of space flight cfDNA concentration in human blood increases several times. The level of cell death in healthy people under extreme conditions is comparable to the level of cell death observed in the exacerbation of chronic diseases, which are accompanied by intense oxidative stress. The chronic effect of relatively small ionizing radiation doses does not lead to blood cfDNA concentration changes. At the same time, the study of the biological cfDNA effects showed that the change in the cfDNA concentration is accompanied by very significant changes in the differentiated and stem cells genomes expression profile. Large cfDNA concentrations have a negative impact on the rheological properties of the blood and contribute to circulatory disorders. Thus, the increase in the cfDNA concentration in astronauts needs to be considered and methods for excessive cfDNA level reduction are to be developed.

TRANSIENT INCREASE IN THE RATE OF CELL RESPIRATION OF MOUSE SPERMATOZOA UNDER EXPOSURE TO SIMULATED HYPERGRAVITY

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Changes in gravitational conditions lead to a number of structural and functional changes in germ cells, in particular in male ones. Nevertheless, the pathways of mechanotransduction in the germ cells remain poorly understood. The aim of this work was to analyze the energy supply of the motility of mouse spermatozoa under altered mechanical conditions.

For 1, 3 and 6 hours, mouse sperm isolated from the caudal epididymis were subjected to simulated microgravity (group 0g) using a random positioning machine and hypergravity using a centrifuge (group 2g), comparing the results with static (CS) and dynamic control (CD). Cell respiration was determined by polarography, where each of the samples at the end of the measurement was tested for the intactness of the mitochondrial membrane by adding 10 μM cytochrome c - all analyzed samples had an intact membrane after permeabilization.

All procedures carried out with animals are approved by the Commission on Biomedical Ethics of the Institute for Biomedical Problems (Protocol No. 521 of September 25, 2019).

Cultivation of spermatozoa under simulated conditions of both microgravity and hypergravity led to a decrease in the number of motile spermatozoa, as well as to a decrease in movement speed, which suggests changes in the energy supply of motor activity. We found no changes in the rate of cell respiration after 1 hour of hypergravity conditions, and after 3 hours, the rate of respiration in the 2g group was significantly higher than in the control. Inhibitory analysis indicates that this increase was due to the more efficient operation of complex I of the respiratory chain, since upon its inhibition and subsequent addition of substrate II of the complex, the rates did not differ from the control. At the same time, it is obvious that a decrease in motility leads to a decrease in ATP consumption and, logically, should lead to a decrease in the respiratory rate. However, the energy supply of spermatozoa occurs, apparently, mainly due to glycolysis. It can be assumed that at the early stages of adaptation to hypergravitational conditions, a transient accumulation of ATP occurs due to a decrease in its utilization, and then the Pasteur effect arises: suppression of the activity of phosphofructokinase under the action of ATP and switching from glycolysis to oxidative phosphorylation; as a consequence, the observed increase in the rate of oxygen consumption. Further, by 6 hours, the expected decrease in the rate of cell respiration occurs, both under conditions of hypergravity and simulated microgravity. Moreover, at the same time, in groups 0g and 2g, there is a decrease in the content of one of the key proteins of the respiratory chain, cytochrome c, and this decrease is most likely due to its proteolysis, since the mRNA content does not change. Thus, taking into account the results of the analysis of cell respiration, the observed changes are likely to be the adaptation of the sperm energy supply system to the new regime of motor activity, but not its cause.

This work was supported by the Basic Research Program of the State Research Center of the Russian Federation - IBMP RAS 65.4 and the Program for Strategic Academic Leadership.

EFFECT OF 3-DAY «DRY» IMMERSION ON THE VEINS CONDITION IN THE LOWER EXTREMITIES OF HEALTHY WOMEN OF REPRODUCTIVE AGE (NAYADA-2020)

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One of the priority tasks of space medicine is to prevent the risk of medical problems in crew members of long-term space missions and to develop specific clinical protocols for medical care. Despite the fact that the physiological effects of prolonged exposure to microgravity and other factors of space flight (SF) on the cardiovascular system have been well studied during 60 years of manned space flights, many aspects of changes in venous hemodynamics and hemostasis require more serious attention of researchers. Earlier, in an experiment simulating microgravity conditions, a case of venous thrombosis of the lower extremities was described [Bleeker M.W. et al., 2004], and in 2019 jugular vein thrombosis was diagnosed in one astronaut on board the ISS, which was followed by successful treatment directly in the SF [Serena M., et al., 2019]. In this regard, it seems especially important to conduct comprehensive studies of the venous system under the effect of SF factors using modern clinically significant methods of examination, and to describe the risk of developing vascular disorders at different stages of SF, taking into account gender differences.

The aim of this study was to assess the effect of 3-day «dry» immersion (DI) on the parameters of venous hemodynamics in women of reproductive age, without the use of countermeasures.

To assess venous hemodynamics in 6 healthy women without bad habits (30.17 ± 5.3 years) in the morning (7 days before the launch of DI, immediately after the end of the experiment, and on the 6th or 7th day of the recovery period) ultrasound angioscanning of the inferior vena cava system according to the clinical protocol (ultrasound scanner Logiq E, GE, USA). The processing of the primary data base was carried out using the Statistica for Windows v. 12.0 (StatSoft, Inc.).

At the moment, the data on the change in the diameters of the vessels of the inferior vena cava system and in the linear bloodstream velocity have been analyzed. A statistically significant decrease in the diameters of the inferior vena cava, common, external, and internal iliac veins was shown at different periods of the examination ($p < 0.05$). At the same time, no significant changes in the linear bloodstream velocity were obtained for the studied veins.

Taking into account that such experiment, with the participation of women in «dry» immersion, was carried out for the first time, we have not found analog studies of the use of ultrasonic angioscanning of the inferior vena cava system in the available medical literature. The data obtained complement the picture of physiological reactions in the early period of adaptation and require the continuation of such studies, including with an increase in the subjects' selection.

SKELETAL MUSCLE TITIN EXPRESSION DURING GRAVITATIONAL UNLOADING

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Under conditions of real or simulated gravitational unloading, atrophic changes occur in the skeletal muscles of humans and animals. These changes are accompanied by increased proteolysis of titin, a giant elastic protein of the sarcomeric cytoskeleton of vertebrate striated muscles. The main functions of titin are to stabilize the sarcomere structure, to regulate the actin-myosin interaction, as well as to impart elastic properties to the muscle, which are necessary for its normal functioning: contraction and stretching. Increased proteolysis of titin under conditions of gravitational unloading leads to a decrease in the content of its full-size (intact) molecules [Udaka et al., J. Gen. Physiol. 2008; Ulanova et al., Biomed. Res. Int. 2015; Ulanova et al., Front Physiol. 2019], which contributes to the deterioration of the contractility of the atrophied muscle. It was found that hyperactivation of calpains, calcium-dependent proteases, is the primary trigger of increased titin proteolysis and a further decrease in its content under conditions of gravitational unloading.

In this work, we investigated changes in the content of titin and its mRNA, as well as possible changes in alternative splicing of titin mRNA, in m. soleus of a rat after seven days of gravitational unloading (hindlimb unloading model). SDS-PAGE using a large-pore 2.3 % polyacrylamide gel fortified with agarose showed a 1.62-fold decrease ($p < 0.01$, $n = 7$) in the content of intact titin molecules (T1) and a 2.1-fold increase ($p < 0.01$) in the content of proteolytic T2- fragments of this protein in atrophied m. soleus of the suspended rats. At the same time, a 4.0-fold decrease ($p < 0.01$, $n = 7$) in the titin mRNA content was found, which was shown by real-time PCR. Long-range PCR and nanopore sequencing revealed an increase in the proportion of shorter titin transcripts in m. soleus of the rats, which can lead to the synthesis of shorter variants of the intact N2A isoform of this protein. In the nuclear fraction of m. soleus of control and suspended rats, no significant differences were found in the content of Rbm20, an RNA-binding protein involved, as shown earlier, in the regulation of alternative splicing of titin mRNA in mammalian cardiac muscle.

Conclusions: (1) along with increased proteolysis of titin, decreased expression of its gene may contribute to a decrease in the content of this protein in rat soleus; (2) along with the decrease in the content of intact titin, induced by gravitational unloading, synthesis of shorter molecules of this protein can occur; (3) Rbm20 does not appear to be involved in the regulation of alternative titin mRNA splicing in skeletal muscle of m. soleus in the rat.

In order to search for measures aimed at reducing unloading-induced atrophy and increased titin proteolysis in rat soleus, experiments on inhibition of histone deacetylases 4 and 5 (regulating gene expression through deacetylation of histones) were carried out against the background of 7 days of gravitational unloading. It was shown that the inhibition of these enzymes largely prevented the increased proteolysis of titin, and also eliminated the decrease in the mRNA content of this protein in m. soleus of the suspended rats.

This work was supported by the Russian Science Foundation (Project No. 18-15-00062).

IMPACT OF LONG-TERM DRY IMMERSION ON SIGNALING PATHWAYS IN HUMAN SOLEUS MUSCLE

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Skeletal muscle is a highly plastic organ, which is able to change its structure and metabolism depending on the mode of contractile activity. Weightlessness leads to a complex of atrophic changes resulting from a significant reduction in muscle

mass and contractile function. Skeletal muscle disuse also leads to a reduction in muscle stiffness and slow-to-fast myosin phenotype transformations. We have previously showed significant changes in muscle signaling pathways in human soleus at the early stage of gravitational unloading. To date, little is known about influence of long-term gravitational unloading on skeletal muscle. The aim of the study was to analyze signaling pathways which regulate myosin phenotype, catabolic and anabolic processes in human soleus muscle under long-term gravitational unloading.

Dry immersion model has been used in order to simulate microgravity conditions. The duration of the dry immersion experiment was 21 days. Using incisional biopsy technique, soleus muscle samples from 8 healthy voluntary males were taken before and after 21 days of dry immersion.

21-day dry immersion resulted in atrophy of both slow and fast soleus muscle fibers. After dry immersion we found a significant decrease in slow myosin mRNA expression and an increase in fast myosin mRNA expression, which were accompanied by a decrease in the nuclear content of NFATc1. We didn't find any changes in E3 ubiquitin ligase MuRF1 and MAFbx expression after 21 days of dry immersion. We observed a significant reduction in p70S6 kinase phosphorylation after 21 days of dry immersion. We also evaluated the content of the key markers of ribosome biogenesis. We observed a significant decrease in the content of 18S and 28S ribosomal RNAs. An expression level of c-Myc mRNA was also declined. After 21 days of dry immersion we observed high-level expression of proinflammatory cytokine IL-6 and its receptor.

Thus, long-term (21 days) exposure of human to dry immersion (gravitational unloading) resulted in a significant atrophy of soleus muscle. The development of the soleus muscle atrophy could be associated with a decline in the markers of protein synthesis, and not with the activation of E3 ubiquitin ligases.

This work was supported by IBMP RAS Basic Research Program (topic 65.3); Russian Science Foundation grant # 19-15-00435.

EMOTIONAL RELATIONSHIPS AS A WAY TO OVERCOME THE ISOLATION STRESS DURING SPACEFLIGHT SIMULATION

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Extreme conditions affect human social behavior. Stress may also promote not only negative or aggressive reactions, but also those characterized by increased prosociality in relation to others, provision of protection and social support. This behavior under stress was labeled as «tend and befriend» response [Taylor et al., 2000]. According to our findings [Solcova et al., 2013] emotional energy proved oneself to be a good indicator of an individual's capability to emotionally invest in relationships with crewmates. From the other hand, during space flight, «in-group favoritism» with the transfer of negative emotions to an external support group is well known as a way to cope with the isolation stress and increase the crew cohesion.

Our research objective was to study the dynamics of emotional relationships in the mixed international crew SIRIUS-19 and, in particular, the «tend ad befriend» phenomenon. We applied the following methods: PSPA computerized test, sociometry, video analysis of group discussions during problem solving. To measure emotional energy, a subscale of Shirom-Melamed Vigor Measure was used.

The results showed that in all women and two men the emotional energy invested in the crew has been high, with small fluctuations in the run of experiment. Crew cohesion, based on reciprocal sociometric choices, increased during isolation as compared to Baseline level. Psychological closeness between the crew members, when measured by the PSPA test as the degree of perceived similarity/difference, also tended to increase throughout isolation. Video analysis of the crew behavior showed that during problem-oriented group discussions they spent more time for emotional interactions than on decision making. At the same time, group effectiveness in problem solving remained at a fairly high level.

We can conclude that in SIRIUS-19 crew emotional relationships, expressed in increased psychological closeness, emotional energy and so-called «tend and befriend» behavior (provision of mutual protection and assistance) represent a dominating pro-social response to a challenging situation of social isolation. In a mixed SIRIUS-19 crew, both men and women showed high levels of emotional energy and social support.

The study was supported by Russian Academy of Sciences, the project 63.2.

INTERPERSONAL INTERACTIONS, COMMUNICATIONS AND GROUP EFFECTIVENESS OF THE SIRIUS-19 CREW FROM INTEGRATED PSYCHOLOGICAL AND ETHOLOGICAL DATA

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Within the frame of multi-disciplinary experiments that the SIRIUS (Scientific International Research In Unique terrestrial Station) project offers, studies need continued sharpening in several areas of data integration for further advances on social behavior in isolated and confined environments (ICEs). The purpose of the "INTERACTIONS" experiment is to study the influence of a mixed crew (gender, age, nationality, profession, etc.) on interpersonal interaction, communication, and group effectiveness under 120-day isolation conditions, simulating extreme factors of long-term space flight (SIRIUS-19). The SIRIUS-19 crew consisted of three men and three women, (men between 31–44 yr of age; women between 29–33 yr of age). One man and all women were Russians, two men were Americans. The related purpose of the «ETHOS» experiment is to study the impact on verbal and non-verbal interactions over time. The main data to assess the crew cohesion measured as the result of mutual sociometric choices in the SIRIUS-19 crew, increased in isolation, compared to the baseline level. Comparison of the significance of individual values (according to the Schwartz' classification) showed that before the start of isolation there were quite pronounced gender differences that tended to smooth out after the end of the experiment, except for values such as Benevolence, Self-Direction and Hedonism, the importance of which remained higher for women than for men. Evaluation of the effectiveness of solving homeostatic tasks showed that a subgroup of men most effectively solved problems of increased complexity. Subgroups mixed in gender composition most successfully solved tasks of medium complexity. A number of significant correlations were revealed between self-esteem, perceptions of some crewmembers and indicators of the psycho-emotional state, which reflects the increased importance of relations with these participants of the crew. It was found that when three crew members (one man and two women) were perceived by others as closer to their ideal, it helped to reduce the level of anxiety and stress. Data visualization and quantification from ethological observations during significant days, support the results and are discussed with regard to behavioral strategies occurred in the dynamics process of adaptation.

ACUTE EFFECT OF HYPER GRAVITY ON THE NEUROMUSCULAR CONTROL IN DROP JUMPS AND DROP LANDINGS

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Introduction: Locomotive movements require precise neuromuscular control and efficient energy management to ensure safe and task-specific movement. Whereas, neuromuscular control is extensively studied during stable gravity conditions on earth, only limited evidence exists addressing the anticipatory capacity and neurophysiological modulations in response to altered gravity. In view of future interplanetary space missions, knowledge of movement control with changes in gravity is required. The ability to ensure efficient energy transfer and safe movement execution has been shown to be particularly challenging under hyper gravity conditions. Therefore, this study aimed to investigate neurophysiological and kinematic modulations during drop jumps (DJ) and drop landings (DL) to gain detailed insight into the acute effects of hyper gravity during parabolic flights.

Methods. DJ and DL were performed in earth gravity (1g, EG) and hyper gravity (1.7–1.9g, HG). In 17 subjects electromyographic (EMG) activity of shank and thigh muscles were assessed before (PRE) ground contact (GC) and during the eccentric phase (ECC). 2D kinematics of the knee and ankle joints and ground reaction forces were recorded to calculate peak forces and leg stiffness. To compare gravity dependent neuromuscular control of both movement modalities, statistical analysis were executed by mixed model ANOVAs (2x2; DJ/DL and EG/HG).

Results. In EG, DJ showed a higher EMG activity in PRE and ECC in the shank and thigh muscles compared to DL indicating task-specific muscle activity. This was accompanied by enhanced peak forces, leg stiffness and reduced knee and ankle joint flexion amplitudes during GC in DJ. In HG, significant interaction effects between gravity and movement modality for PRE indicate enhanced neuromuscular activity before GC in both, DJ and DL. During ECC, the neuromuscular activity demonstrates

an opposite modulation; whereas it was reduced in DJ, neuromuscular activity was increased in DL. Peak forces, knee and ankle joint flexion amplitudes during GC were significantly increased in both DJ and DL.

Discussion and Conclusion. Both movement modalities show task-specific neuromuscular activity in EG characterized by high PRE and ECC EMG for DJ, whereas DL require less neuromuscular activity in PRE and ECC to dissipate energy. During HG, the enhanced neuromuscular stiffness before GC, for both DJ and DL, underlines the anticipatory capacity of the central nervous system to prepare for increasing gravitational load. This appears to be essential to resist the extensive impact forces during HG. Contrarily, neuromuscular activity during ECC seems to be converging between DJ and DL. In order to dissipate high impact forces during DL, increased neuromuscular activity and leg stiffness is required. During DJ, decreased neuromuscular activity and increased knee and ankle joint flexion amplitudes are indicative for a more compliant system. This could represent a preventive strategy in HG to protect musculo-skeletal structures from exceeding common muscle-tendon safety factors. In summary, this study demonstrates that movement control can be modulated in a task-specific manner beyond EG, whereas in DJ the prerequisites for a highly efficient energy management seem to be negatively altered to ensure safe movement execution.

NASA HUMAN RESEARCH PROGRAM – OVERVIEW OF BEHAVIORAL HEALTH AND PERFORMANCE RESEARCH IN THE SIRIUS ANALOG

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Future exploration missions to Mars will require extended duration to and on a distant planetary surface, exposing crews to multiple hazards: galactic cosmic radiation, distance from earth, isolation and confinement, hostile closed environment, and altered gravity. The Human Factors and Behavioral Performance Element (HFBP) in the NASA Human Research Program (HRP) supports and manages research to characterize and mitigate the effects of these hazards on crew behavioral health and performance. HFBP research relates to five human health risks, including the Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team («Team Risk») and the Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders («BMed Risk»).

To prepare for these missions, research is needed to understand the effects of the hazards, including the potential synergistic effects of exposure to multiple hazards, and to evaluate the effectiveness and acceptability of targeted countermeasure strategies. Hence, HFBP uses multiple platforms to address specific research questions. For research related to the Team Risk, for example, little is known about team processes over time, particularly under conditions of isolation and confinement, and with additional stressors including heavy workloads, sleep deprivation, and communication delays. The SIRIUS facility at the Institute for Biomedical Problems (IBMP) provides a rich opportunity to assess and evaluate teams over time, and to determine optimal countermeasures for supporting future crews. The ability to investigate individuals in prolonged isolation also allows for an assessment of potential behavioral health decrements—as needed to address the BMed Risk—and to understand the 'dose response' effect of time, on individual and team health and performance outcomes.

HFBP therefore initiated a cohort of investigations to take place at the SIRIUS facility, for various durations, to investigate whether outcomes seen over shorter time periods hold true or change for extended durations. This presentation will provide an overview of these studies and how HFBP has partnered within HRP and with the IBMP, to ensure high fidelity of the SIRIUS missions to future spaceflight. By ensuring a consistent, high-fidelity environment, mission scenario, and crew, we can try to isolate the effects of time on various individual and team health and performance outcomes, thereby informing our collective approach towards protecting and enabling future crews on a mission to Mars.

It is recommended that this presentation, if selected, precede several other presentations from HFBP-HRP funded investigators, who will provide more details on the implementation and results of their SIRIUS studies.

LINKING BIOMEDICAL RESEARCH AND TECHNOLOGICAL INNOVATION FOR HUMAN HEALTH IN SPACE AND ON EARTH – OVERVIEW OF CURRENT PROJECTS AND FUTURE PLANS IN THE :ENVIHAB

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The :envihab, composed of the words «environment» and «habitat», is a unique medical research facility operated by the DLR Institute of Aerospace Medicine. Since 2013 :envihab serves as a platform for many studies and projects, most of them to explore effects of extreme environmental conditions on humans and to develop effective countermeasures. Several mechanism-oriented sleep studies as well as bed rest stu-dies up to 60 days have been successfully completed in :envihab, mainly functioning as so called Space Analog.

Within its eight modules, :envihab houses multi-purpose laboratories and specialized equipment for life science research. Furthermore, :envihab features a high-end research ward accommodating study partici-pants in bed rest studies and sleep

investigations among others. The module comprises 12 individual rooms and can be conditioned using normobaric hypoxia or hypercapnia. :envihab offers a fully equipped human short-arm centrifuge enhanced for example with a robotic-controlled ultrasound device and a Vi-con motion capturing system for numerous research opportunities, including the exploration of training options under different g-conditions. The 3 Tesla PET-MRI allows for sophisticated structural, functional, and molecular imaging. The Biology Lab consists of four microbiology laboratory rooms, one of them be-ing an ISO class 8 clean room. A large hypobaric chamber is suitable for hypobaric hypoxia, normobaric hypoxia, and hypercapnia studies. Finally, advanced cardiovascular, musculoskeletal, metabolic, ophthal-mological, and psychological testing as well as highly controlled dietary support make :envihab a world-wide unique human research facility.

The Institute also supports postflight activities of ESA astronauts – the so-called «Direct Return». Astro-nauts, crew surgeon and operational staff can be easily accommodated in :envihab. The Crew Quarters are access-controlled for infection control and astronaut privacy. All medical pre- and post-flight examina-tions required according to the Medical Standards for Crewmembers as well as some pre- and post-flight experiments are conducted within :envihab.

Currently, more bed rest studies in cooperation with NASA are prepared as well as, e.g., different studies under hypoxic conditions. Plans for future studies with different topics over the next five years, including more bed rest studies, are already made. In addition, the LUNA Habitat which will soon be constructed next to :envihab, will broaden the range of research opportunities from human spaceflight to planetary exploration, like future lunar missions in cooperation with ESA. Overall we very much welcome additional international cooperation.

BENEFITS BEYOND: MINDFUL MISSIONS IN AUTONOMY CREATING AN ADAPTIVE EXPERIENCE THROUGH MOVEMENT

Winters A.

As research on the health and safety of humans in long duration space missions supporting exploration continues, new ways to mitigate space sickness to support crew well being and mission success are essential. This paper examines the physiological cost of space travel, as well as adaption techniques discovered and experimented to mitigate the negative impacts on humans for long term, sustainable spaceflight for planned lunar and Mars missions. The research was inspired by cooperation of international efforts to benefit those on Earth and beyond, to increase the ability to live and work sustainably in space. Developing and emerging space nations are encouraged to support the partnership through collaboration on the topic of increasing individual and crew performance through an astronaut/ cosmonauts physical and mental health. Behavioral science assessments and adaptation techniques are discussed to highlight the link between physiological states and the performance of crew tasks. By evolving latent natural human potential through exercise, timely autonomous decision making becomes a major component of risk prevention in challenging contexts. Innovative concepts on emotional regulation, isolation, reduction in depression and anxiety are taken into consideration to include VYT (Vestibular Yoga Training), ACT (Acceptance and Commitment Therapy), DBT (Dialectal Behavioral Therapy) and other CBT (Cognitive Behavioral Therapies) as a combination of exercises will need to be applied and evaluated to mitigate issues associated with space sickness. Stabilization of vital signs through mindful movements and breathing techniques define the parameters of progress, underlining the importance of cognitive performance insight. The prevention and management of medical contingencies aboard the spacecraft is essential for improved medical autonomy of the crew and ensuring greater mission success. This integrated approach to human health not only increases the vitality and social resilience of crew performance, but the safety of space exploration as a whole. By supporting persistent survival techniques through the experience of completing meaningful tasks and harnessing the abilities of self awareness, humans can live and work effectively together more successfully in space.

MITIGATING THE EFFECTS OF SPACE ADAPTATION THROUGH VESTIBULAR YOGA TRAINING

Winters A.

Altered vestibular functions due to the free-fall environment of space travel have plagued astronauts since the beginning of the space age. These effects can range from minor annoyance and impairment to complete debilitation. Fortunately most astronauts adapt, to some extent, to this environment within a few days. Upon returning to earth, they then need to re-adapt to a 1G environment. This paper will examine vestibular yoga training (VYT) as a method for reducing free-fall adaptation time, the 1G re-adaptation time, and as a new risk prevention approach to mitigate spaceflight associated neuro-ocular syndrome (SANS) and (VIIP) visual impairment due to intracranial pressure. Vestibular Yoga Training consists of a series of yoga derived postures and breathing techniques combined with coordinated eye movements, originally designed to help individuals who suffered from vestibular stress or individuals that are recovering from vestibular damage due to accidents,

aging, or other health related issues. VYT enhances the central nervous system's capacity to compensate for inner ear and functional deficits that lead to balance disorders. Combining optical nerve retraining, peripheral vision exercises, along with yoga poses that emphasize strengthening and alignment, VYT improves neuromuscular coordination while restoring inner and outer balance. A proposed focus area for further research is on the potential for improving spaceflight associated neuro-ocular syndrome (SANS) and (VIIP) visual impairment due to intracranial pressure. VYT has shown to promote an increase in sensory function and fine motor skills. Improvements are gained through the alignment of multiple systems in the body to include musculoskeletal, respiratory, circulatory, in addition to vestibular benefits. This paper begins with a brief review of the vestibular system and the effects astronauts experience in the free-fall environment, followed by a description of VYT and proposed design of experiments to test SANS/VIIP risk prevention. A series of ground-based and space-based experiments are discussed to quantify the beneficial effects of VYT for reducing the time for astronauts to acclimate to the free-fall environment during early mission phases, but also to re-adapt to 1-g upon return to earth. The paper concludes with a proposed research program-including hypotheses and VYT regimens- to investigate how VYT could be used by astronauts to mitigate space adaptation through vestibular yoga training.

E-NOSE TECHNIQUE APPLICATION IN THE DIAGNOSIS OF PNEUMONIA

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Acute respiratory infections are common, with an average of 2-4 episodes per year in adults and 6–8 episodes per year in children. Most of these respiratory infections are not caused by bacteria, which can be treated by antibiotics, but by virus, where antibiotic treatment is ineffective. However, antibiotics are often prescribed despite the causative pathogen has not yet been identified at the time of diagnosis. Approximately half of the 40 million outpatient antibiotic prescriptions made in the USA for the treatment of respiratory infections are considered unnecessary, and contribute to increased rates of multi-resistant bacteria and other side effects. This highlights the need of a reliable diagnostic method for the rapid discrimination between bacterial and viral respiratory tract infections. Infections have shown to alter the composition of volatile organic and non-organic compounds (VOC) in exhaled air. Bacteria release characteristic VOCs as part of their metabolism, while viruses infect their host's cells and alter the VOC composition through influencing the host's metabolism.

Using highly sensitive analytical platforms, characteristic VOC signatures can be detected in exhaled air, provide insight into the patient's metabolic processes and in case of infection, should allow for identification of the underlying microbial pathogen. In the clinical setting, breath gas sampling presents a non-invasive procedure with no relevant risk or discomfort for the patient, allowing for repeated sampling and high patient compliance.

Thus, we currently conduct a non-interventional, non-randomized, open prospective observational study utilizing E-Nose technology (E-Nose and Enrichment & Desorption Unit) to examine the breath gas of patients with bacterial or viral pneumonia. We aim to establish E-Nose technology as a reliable tool for discrimination between patients with bacterial or viral respiratory tract infection, and potentially identify VOC signatures that allow for an even more specific differentiation of the causative bacteria or virus, e.g., to distinguish influenza virus pneumonia from SARS-CoV-2 pneumonia.

Compared to other detection methods like gas chromatography-mass spectroscopy (GC-MS), monitoring breath gas with E-Nose technology has several advantages. Due to the small size, the E-Nose system can be easily applied within a hospital setting, but also serve as a portable diagnostic unit at remote locations. The equipment is robust and analyses can be carried out without the need of laboratory support, as it is required for blood or bacterial culture analyses. Due to the low amount of consumables and reagents, this method is very cost effective, and results are available within 20 minutes, enabling the patient to receive the optimal therapy in a timely manner.

The urgent need for rapid, non-invasive and cost-effective diagnostic tools together with the pathomechanisms of VOC alteration during infection emphasizes the high potential for a translational application of E-Nose technology from Space applications to the medical setting.

MOLECULAR BIOMARKERS OF SUSCEPTIBILITY FOR LATE-ONSET NEUROPATHOLOGIES AND MULTIVARIATE MODELING OF INDIVIDUAL RISKS FOR OPERATION-RELEVANT BEHAVIORAL DEFICITS AFTER EXPOSURE TO SPACE RADIATION

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Exposure to deep-space radiation has consequential risks for persistent CNS tissue damage and behavior deficits. In rodent models, simulated space radiation can induce a broad range of molecular, cellular, neurocognitive, behavioral, and tissue pathologies. Our hypotheses are that: (i) the nature of early molecular responses and cellular damage in brain sub-regions is predictive for risks for late-onset CNS pathologies, and (ii) individual-level risks for operation-relevant behavioral performance can be estimated from multivariable models that incorporate exposure variables, as well as individual-specific molecular biomarkers, cellular biomarkers, and genetic/physiological effect modifiers.

Brain sub-region multi-omics predicts late-onset CNS pathologies. Exposure of male rats to ^{56}Fe induced multi-omic changes in cerebral spinal fluid and brain sub-regions that were associated with diverse tissue damage functions. Histological inspection of the brain tissue from ~4 to ~22 months after exposure confirmed several predicted categories of damage but with differing delays in post-exposure onsets, including endothelial vascular fibrosis, damage to the choroid plexus (CP) epithelium, and increased amyloid burden (Congo Red, betaA4, and Ttr amyloids). Our findings suggest that CP and CSF are radiation-sensitive targets associated with risks for late-onset CNS pathologies.

Predictive modeling of individual risks for radiation impact on operation-relevant performance. The effects of cosmic radiation on operation-relevant behavior performance are expected to vary with the nature of the exposure, the genetics and physiology of the individual at the time of exposure, individual variations in the CNS damage response functions, and persistence of tissue damage functions with time after exposure. Understanding the associations between exposure regimen, molecular and cellular biomarker changes, and behavioral endpoints are important for building predictive models of individual-level risks for operation-relevant performance. We have identified panels of hippocampal and CP proteins that were differentially associated with anxiety behavior performance on the elevated plus maze. Affected proteins were associated with upstream regulators of certain neurological diseases, and with tissue function typically associated with persistent neurotoxicity, such as oxidative stress and immune dysfunction. We are evaluating CNS protein responses and radiation-induced behavior deficits in rodent models to build a suite of multivariate models to be evaluated for predicting individual risks for anxiety and other operation-relevant performance.

Impact. Our goal is to advance the development of mechanistic and kinetic models of molecular changes in CSF, CNS regions, and peripheral blood over time after exposure, and to build computational models to predict individual-level risks for behavior deficits and neuropathies associated with neurological diseases. These projects are designed to reduce the uncertainty associated with assessing and predicting the CNS risk for deep space missions.

FEATURES OF HEART RATE VARIABILITY AND MYOCARDIUM ENERGY METABOLISM IN SPACE FLIGHT

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Reputedly, that electrocardiogram's changes during a long-term space flight indicate the energy-metabolic shifts in the myocardium. These changes are not clearly reflected in the traditional electrocardiographic study and require special research.

In 16 Russian cosmonauts, a study of the features of the regulation of the heart rate and electrophysiological changes in the myocardium in space flight was carried out. The scientific concept of the investigations is based on the theory of electrophysiological characteristics of the myocardium as indicators of energy and metabolic processes on the cell level; the role of energy characteristics of the heart in maintaining cardiovascular homeostasis in space flight and, in particular, in the period of re-adaptation; an association between energy and metabolic processes in the myocardium with autonomic regulation of circulation.

With prolonged action of weightlessness, a change in the autonomic balance towards an increase in sympathetic activity is observed, with a decrease in the functional reserve of regulatory systems and a change in the electrophysiological properties

of the myocardium. The diurnal dynamics of the indices of autonomic regulation correlates with diurnal changes in the electrophysiological characteristics of the myocardium and can serve as an indicator of the body's adaptive reactions.

According to our point of view, the initial manifestations of electrophysiological remodeling arising under conditions of prolonged weightlessness can be no less significant causes of the development of orthostatic instability than changes in vascular tone.

The study was carried out within the framework of the basic theme of RAS 64.1 for 2013–2023.

SUBJECTIVE PERCEPTION OF TIME IN SPACE FLIGHTS AND ANALOGS: STUDY METHODS

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There are two main focuses in studies of time perception in extreme environments. The first one is time intervals perception analysis, aiming to know if short time intervals, such as seconds and minutes, are perceived faster or slower. These studies are important for cosmonauts experiencing overload and performing docking and other precise and timely activities, and are connected with research on reaction time. The second one targets long-term processes, such as months and years, to understand how personal perception of time changes under stress and monotony: if time runs fast or moves slowly while a person is in long-term isolation.

While analysis of short time intervals shown connections between overloads and time perception as well as with individual nervous system reactivity, analysis of time perception in long isolations mainly based on anecdotal reports. Choice of methods to be used for time perception analysis in long-term isolation is not evident: time perception inventories mostly look at lifetime analysis and retrospective memory. While anecdotal reports and self-reports still are a source of data, we may consider speech as a possible source of data on time perception in long-term missions.

In Content space experiment held on Russian segment of International Space Station since 2015, we analyze cosmonauts' conversations with Russian MCC using content analysis. While our main focus during this experiment was on stress coping strategies, we also collected data on Time category in speech. We counted all statements that indicated a lack of time (for example, as a request or a confrontation) or excess of time, as well as time expenditures – including those that are useless / meaningless from the point of view of the speaker, and transfer of affairs to another time period.

The data we acquired showed use of this category, i.e. all mentions of time, in speech of 15 Russian cosmonauts during their flights. We compared category variation in different subjects with V. Satir's communication styles we discovered earlier and found that subjects with different communication styles show different distribution of time category use in flight. However, the quantitative distribution analysis would be incomplete without qualitative analysis of statements used by subjects with different styles. Mixed analysis method shows how subjects with different communicative styles relate their workload with time. Sequential qualitative analysis of statements allows to better show emotional aspects of analyzed speech and get a clearer image of subjects' relations with time in space flight.

The study was supported by the Ministry of Science and Higher Education of the Russian Federation under the agreement No. _075-1502020-919 from 16.11.2020 about the grant in the form of subsidy from the federal budget to provide government support for the creation and development of a worldclass research center «Pavlov Center for Integrative Physiology to Medicine, High-tech Healthcare and Stress Tolerance Technologies».

PHARMACOLOGICAL INDUCTION OF HYPOBIOSIS: TRENDS AND PROSPECTS. PART I. REVERSIBLE TORPOR AND HYPOTHERMIA

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To initiate a state of artificial torpor, we suggested a pharmacological multi-targeting strategy for the simulation of the physiological pattern of natural hibernation including a significant reduction in heart rate, respiratory rate, body temperature, and oxygen consumption as well as a decline in brain activity known as torpor [1]. For this purpose, we have developed a composition which initiates a pharmacologically induced torpor like state (PITS-composition), made up of eight therapeutic agents, inert gas xenon and lipid emulsion served as a drug vehicle. It was found that after a single intravenous injection to rats, PITS-composition causes a rapid decline in heart rate followed by a steady decrease in body temperature from about

38.5 °C to 30.5 °C, at the ambient temperature of 22°C–23°C. The hypothermic state may continue on average for 16–17 h with the subsequent spontaneous return of heart rate and body temperature to the initial values.

PLANETARY BASE AUTOMATED CONTROL SYSTEM

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The planetary base deployment (Moon, Mars, etc.) is a high priority task for space exploration. As of now, the practical results of planetary base's automated control system (PB ACS) creation are insufficient. Using the experience of developing an ACS of life support systems complex (LSSC).

The ACS's modules main purpose correlates with their respective names:

– ACS Crew – information database on crew members (location, routes, schedule, etc.);

– ACS Space –outer space monitoring (radiation, etc.) and emergency response unit;

– ACS Transport – logistics' infrastructure control on the planet's surface;

– ACS Spaceport – landing and launch procedures management for manned and unmanned spacecraft.

When creating an electro-technical network for a PB, a single-wire power transmission based on the ideas of N. Tesla is promising. This will provide a high safety and reduce the mass and overall size of the cable network and the losses during power transmission.

Conclusion:

– The structure of the PB ACS is described.

– The electrical engineering principles by N. Tesla are proposed for the electro-technical network of the planetary base.

– In the future, it is required to develop the ACS for individual modules as part of the PB ACS.

ROLE OF ATP-DEPENDET SIGNALLING IN RAT SOLEUS MUSCLE UNDER HINDLIMB UNLOADING

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Skeletal muscle is a highly plastic tissue that can adapt its structure and metabolism in response to various conditions. Under unloading condition, skeletal muscles undergo atrophy due to a decrease in protein synthesis and/or an increase in protein breakdown. Recent studies have shown that the changes in intracellular signaling pathways occur in first days, and even hours of muscle unloading (Mirzoev TM, Shenkman BS, 2018). It is known that during muscle unloading, macroergic phosphates (ATP, PCr) and Ca ions accumulate in muscle fibers (Ohira Y et al., 1994, Shenkman BS, Nemirovskaya TL, 2008). It has been shown previously for many tissues that extracellular ATP is the main autocrine-paracrine mediator for cell signaling caused by hormones, growth factors, neurotransmitters, mechanical stimuli, and inflammation (Lazarowski ER et al., 2003). Therefore, we suggest that ATP may be the central integrator of all stimuli obtained for skeletal muscle cells in order to allow and coordinate events for the expression of muscle genes. The purpose of our work is to identify the source of entry, transmission paths, and the effects of these incentives.

We hypothesized the mechanism of this process: ATP from the muscle fiber can efflux through pannexin channels (pannexin-1; PnX1) to the extracellular space upon muscle unloading. These nucleotides can then interact with P2Y channels, (G protein Y-coupled receptors), which in turn activate the PI3 gamma kinase (PI3K) (in the T-channels of the membrane and, ultimately, IP3 receptors located in the nucleus and sarcoplasmic reticulum). Activation of IP3 receptors (IP3R) can cause a weak signal of calcium release, both cytosolic and nucleoplasmic, which promotes (possibly with other signaling cascades) activation of transcription factors, which leads to the increase or decrease of expression of genes involved in muscle phenotype. We tested this hypothesis by applying in the model of hindlimb suspension of rats the inhibition of pannexin channels (PnX1) that efflux ATP from the cytoplasm into the extracellular space. For the experiment, 24 male Wistar rats weighing 180-220 g and 12 weeks of age were taken and randomly distributed into 3 groups (8 rats in each): group C – intact control, group 3H – 3-day hindlimb suspension with placebo administration; group 3P – 3-day hindlimb suspension with per os probenecid (PRB) administration (50 mg/kg daily per os by gavage. The daily dose was administered in two divided doses 12 hours apart. A significant increase in the amount of ATP (by 32 %, $p < 0,05$) in m. soleus of rats was found during 3-day suspension (relative to the control group). Inhibition of pannexin channels in gr. 3P led to an 19% greater accumulation of ATP in the soleus muscle. It was found in 3P group: 1. mRNA expression of E3 ligases MuRF1 and atrogen-1 was significantly lower (by 50 and 38 % respectively) than that in the group without channels inhibition, 2. the content of phospho-p70S6k and phospho-p90RSK were significantly higher (by 51 and 35 % respectively), and phospho-eEF2 (suppressing elongation) was

significantly lower than those in the group without pannexin channels inhibition upon hindlimb suspension ($p < 0,05$) and was similar to that of control group. The level of phospho-GSK3β was 189 % higher than in 3H group.

Conclusion. We found for the first time that ATP-dependent transport in skeletal muscle (via pannexin channels) is involved in the regulation of the expression of E3 ligases, and also enhances translation processes and prevents a decrease in elongation in m.soleus upon hindlimb suspension of rat. This work was supported by the RFBR grant No. 20-015-00138.

SENSORIMOTOR TASKS DURING 21-DAY DRY IMMERSION

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Changes in the activity of afferent systems and their interactions at simulated microgravity have a significant impact on the formation and implementation of motor programs, causing the development of disorders in the mechanisms of posture control, locomotion and voluntary precision movements (Kozlovskaya et al., 1987). Previously, the trigger role of support unloading at dry immersion (DI) in these violations was shown (Kozlovskaya et al., 2007). The dynamometry as well as tracing and grasping tasks allow assessing the overall characteristics of precision arbitrary hand movements (Sosnina et al., 2018, 2021).

Ten volunteers performed different sensorimotor tasks before DI, at 3^{d}, 10th and 20th day of DI and after its accomplishment. They grasped by their dominant hand the upper and lower rod consisting the central part of stimuli that elicited the Muller-Lyer and Ponzo illusions. They traced by index finger of their dominant hand the upper and lower shaft consisting the central part of images that elicited the Muller-Lyer and Ponzo illusions with and without visual feedback. They successively compressed the dynamometer in such a way that each subsequent force exceeds the previous one in amplitude with a minimum difference between adjacent forces.

The abovementioned tasks results showed different dynamics during DI. The strength of both illusions stayed unchanged during presumably the simplest task, namely, tracing with the visual feedback. The differential threshold measured by dynamometer diminished in DI relative to initial values. The strength of Muller-Lyer illusion during tracing without visual feedback diminished in the middle of DI than it increased and then decreased again down to zero. The strength of both illusions during grasping without visual feedback diminished in the beginning of DI than it increased in the middle of DI and then decreased again. Meanwhile the strength of illusions at tasks with visual feedback, i.e. without the use of visual memory, correlated with the differential force threshold when mean threshold was minimal (3^{d} and 20th days of DI). The strength of both illusion at grasping correlated with the differential force threshold in 3^{d} day of DI: the stronger the illusions were the lower the threshold was. The same direction of correlation between the strength of Ponzo illusion during tracing without visual feedback and the differential force threshold was observed in 3^{d} and 20th days of DI.

The results received may be interpreted in favor of strengthening the influence of dorsal pathway of visual processing relative to the ventral one. This strengthening leads as to increase of sensitivity to force threshold as to decrease of visual illusions' strength. The changes in sensorimotor tasks performance due to gravitational unload are prolonged what should be taken into account when planning both experimental studies and real operations of astronauts in orbit. The proposed techniques can be used in studies of gravitational unloading to assess the effectiveness of sensorimotor coordination.

The work is supported by RFBR grant 19-013-00036.

DYNAMICS OF THE FUNCTIONAL ACTIVITY OF THE RETINA AFTER FOUR MONTHS OF ISOLATION IN A SEALED OBJECT SIMULATED A SPACE FLIGHT

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Introduction. Long-term flights' success depends, among other things, on predicting human performance in stressor conditions. The preservation of the functionality of the sensory systems implies a high-stress resistance. The urgent task is to study adaptation mechanisms that fit the visual system's functioning with the extreme environment's conditions. In the experiment, SIRIUS18/19, an electrophysiological study of the visual system was carried out to expand ideas about its stability in complicated situations.

Purpose. To obtain new objective data on the alterations in the visual system's functional activity during the prolonged human stay in extreme environmental conditions.

Material and Methods. Before and after a 4-month isolation experiment simulating a flight to the moon, full-field electroretinograms (ERGs), pattern ERG (PERG), and pattern-reversal visual evoked cortical potentials (VEPs) were registered according to the ISCEV Standards in six practically healthy crew members. The retinocortical time (RCT) was calculated as a difference in the peak latency of the P100 VEP and the PERG P50 peak.

Results. A general tendency included a slight decrease in the amplitude of the P50 and N95 PERG, flicker ERG and P100 VEP peaks after the experiment. However, there were no statistically significant differences in the retina and visual cortex activity from the initial data. In three pilots, we revealed specific alterations of the ERG and VEP responses to small patterns stimulating the visual system's parvocellular channels.

Discussion. The PERG P50 and N95 dynamics indicate a slight decrease in the function of spiking and non-spiking ON- and OFF- retinal neurons. The stability of RCT, reflecting the time of excitation from the retina to the primary visual cortex, indicates the integral preservation of the visual pathways. In three pilots, a more significant decrease in the P100 VEP amplitude for patterns 0.3°, which characterize the parvocellular visual channels' activity, was found compared to other crew members. These testers included the captain and flight engineer - the persons whose duties on board assumed the highest personal responsibility. Moreover, throughout the experiment, they regularly engaged in active physical training (simulators and boxing). Their VEP changes were associated with higher visually intense work and physical activity and with an individual reaction to sleep deprivation under increased responsibility.

Conclusion. Four-month isolation with imitation of a space mission did not cause significant changes in the retina and visual pathways' functional activity in healthy crew members. Specific differences of VEP-responses of the parvocellular visual system were revealed in physically active crew members, reflecting a high level of their psychophysiological adaptation and stress resistance.