# 3. LIFE SCIENCES.

The collaboration of the ***Institute of Experimental Endocrinology, Slovak Academy of Sciences, Bratislava***, (IEE SAS) and Faculty of Medicine, Lyon, France facilitated the participation of the IEE, SAS on the project of ESA performed on the studies of the effects of the exposure of human subjects to long term bed rest. Besides the scientists from the countries of ESA, also the research teams from USA (NASA) from Japan (NASDA) take part on this project. In IEE SAS the project: Mechanisms of Neuroendocrine, Cardiovascular and Metabolic Adaptation to Simulated Microgravity is performed. Head-down bed rest (HDBR) has been a model commonly used to simulate the effect of weightlessness. Studies of HDBR of various duration have been performed and improved the knowledge of the influence of microgravity, mainly concerning the alterations of cardiovascular system. In our previous investigation during short space flight and HDBR was found that neuroendocrine and metabolic responses to various stressors in the same subject differ from those obtained under normal gravity. Prolonged space flights or stay on ISS require prediction the responses of the organism to various stressors during the process of adaptation to weightlessness by using the results of observations in subjects exposed to simulated microgravity. The overall objective of this proposal is to investigate neuroendocrine, cardiovascular, metabolic and immune responses to mental and somatic stressors acting by different mechanisms (metabolic, cardiovascular, physical) during HDBR of various duration simulating a stay of microgravity. Responses to stress stimuli are supposed to be determined during pre-bed rest period and at various intervals of HDBR.

The results of these studies should lead to a new understanding of the relationship between circulatory, neuroendocrine and metabolic mechanisms involved in adaptive changes during microgravity and provide the means of compensating or accounting the undesirable development.

The collaboration of the ***Institute of Experimental Endocrinology, SAS*** and Faculty of Medicine, Lyon, France is concentrated on the determinations of plasma and urinary catecholamines and their metabolites during and after the exposure to long term bed rest. The samples of blood and urine from persons exposed to long-term bedrest are analyzed for catecholamine contents in IEE SAS.

The agreement on the collaboration between IEE SAS and Institute of Biomedical Problems of State Research Center, Russian Academy of Sciences, Moscow, was signed in 2001. By using the complex of appliance PLASMA 03

the investigation of the neuroendocrine response to workload, metabolic and psychic loads will be determined with participation of scientists from both Institutions. IEE SAS will also participate on regular investigation of health status of astronauts during long term space flights. The project *Responses of human organism to different loads during long-term space flight on ISS - Endotest 2* is performed under this collaboration. The project is aimed to study neuroendocrine, metabolic and cardiovascular responses of astronauts to different loads during long-term stay in space, the adaptation process of physiological functions, to judge possible negative effects of stay in space on human organism and to design precautions.

In our previous investigations in Slovak astronaut (program *Štefánik*) were found significant differences in neuroendocrine reactivity to various loads during short-duration space mission compared to pre- and post-flight conditions - exaggerated response of stress hormones during physical exercise and mental stress and diminished contraregulatory response to lowering of blood sugar, which is the essential fuel for brain. These alterations might be due to countercharge of neuroendocrine system to acute change of gravity and it would be necessary to elucidate the chronic effects of "zero" gravity.

In majority of previous studies during long-lasting space missions, the data describing the levels of hormones and metabolites and the parameters of body fluids balance were obtained in steady state conditions. Functional loads were used to study presumably the markers of cardiovascular system (changes of heart rate, blood pressure, peripheral vascular resistance etc.) and no data were collected about the changes of levels of hormones and metabolites, which allow to determine the level of load, the tolerance interval to load, the adaptability to load and the organism ability to cope with physical and mental demands of life on the board of space station with enhanced potential of acute, not expectable situations, which may have stressogenic influence on astronaut organism.

The presented project supposes to determine the dynamic function tests for evaluation of physiological responses in pre-flight period, on the beginning of the space stay, at the end of 4-months space flight and during re-adaptation after landing. These include neuroendocrine, circulatory and metabolic responses to physical exercise, insulin sensitivity, mental performance and associated neuroendocrine and cardiovascular activation during all periods and responses to orthostatic test during pre-flight and post-flight period.

The obtained results will extend the knowledge of physiological adaptation to space flight and evaluate the ability of the human body to respond properly on different stress situations. This integrated insight will allow to predict potential

problems, and plan adequate responses to situations that might occur during long-term missions.

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The Project *Influence of simulated microgravity on human postural responses to sensory stimulation* is performed in the ***Institute of Normal and Pathological Physiology, SAS , Bratislava***. The aim of project is the investigation of the role of altered sensory interaction in postural instabilities after spaceflight to test "reweighting" of vestibular and somatosensory inputs by postural responses to galvanic vestibular and muscle vibratory stimulation. Activity in 2001: Balance test data of Slovak cosmonaut recorded after short spaceflight were analyzed in relation to transient postural instability after landing. The results confirmed that sensory interaction altered in microgravity is likely responsible for the post-spaceflight balance instability. On the basis of these results, we improved galvanic balance test, which allow to estimate the altered weight of vestibular input in human balance control during re-adaptation to Earth's condition.

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In Space Biology the project *Changes of functions of neuroendocrine system during exposure to simulated microgravity and hypergravity* is performed with the participation of several Institutes, namely ***Institute of Experimental Endocrinology, Slovak Academy of Sciences, Bratislava, Slovakia, Institute of Animal Biochemistry and Genetics, Slovak Academy of Sciences, Ivánka pri Dunaji, Slovakia, Institute of Measurement Science, Slovak Academy of Sciences, Bratislava.*** The aim the investigations in proposed project is realization of the series of the experiments with rats exposed to hypokinesia (tail-suspension hypokinesia, restriction of mobility) for various time period with the blood sampling during the hypokinesia by using a canula and determination of plasma levels of hormones, neurotransmitters and metabolites. In selected time intervals it is proposed to measure in isolated organs and tissues the content of neurotransmitters, hormones, production of hormones, activity of enzymes involved in the production of neurotransmitters, expression of genes for coding these enzymes. The response of neuroendocrine system (changes of catecholamine, corticosterone, prolactine, growth hormone) will be determined. The results will be used for evaluation of the capacity of the organism to overcome several stress loads.

Similar protocol of observations is proposed for the group of animals exposed for a short time to hypergravity (by using centrifuge device in the Institute of Animal Biochemistry and Genetics, SAS, simulating a gravity load at start or landing of space satellite (6-8 G). Also the studies of adaptation to hypergravity of 2 G for the period of two weeks, simulating the process of postflight readaptation, are proposed. The results of these experiments are important for the understanding of the mechanism of the changes of the activity of neuroendocrine system and metabolic processes observed in human subjects and experimental animals after space flights, and also to distinguish between specific effects of microgravity, hypergravity during the landing and postflight readaptation to gravity conditions on Earth.

For these studies an Electronic Equipment for Multiple Blood Withdrawal with Telemetric Control from small experimental animals has been developed and tested (Figure 6 ). A pair of rats is placed in a box rotating in a centrifuge with maximal 6g gravitational overloading. The equipment consists of a telemetric transmitter (placed outside the room of the centrifuge) and receiver. Both transmitter and receiver are equipped by microcomputers. It is also possible to measure the instantaneous gravitational force using an accelerometric transducer placed near the box with telemetric data transmission.

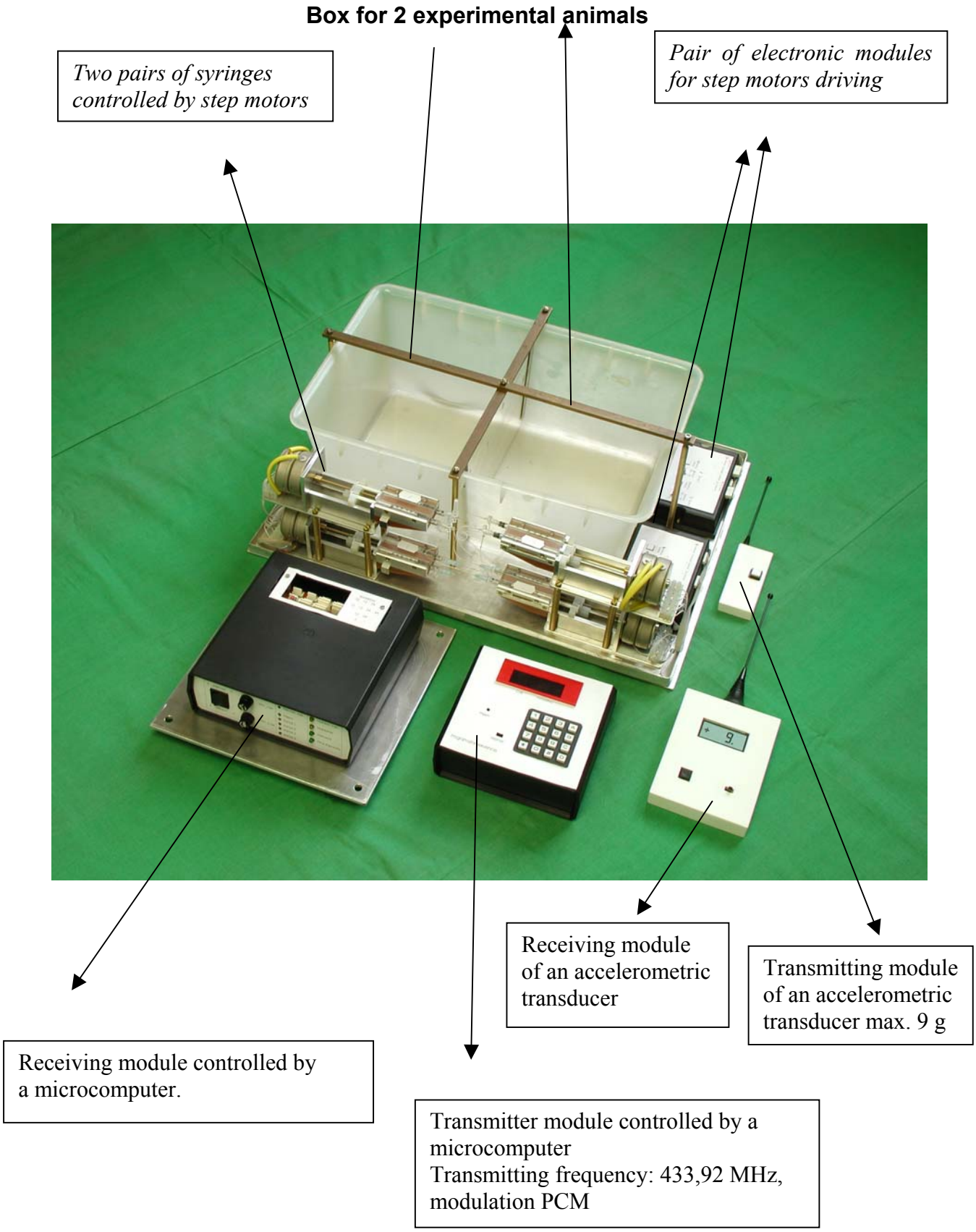


*Fig. 6. Electronic equipment for multiple blood withdrawal with telemetric control. Developed by the Institute of Measurement Science, SAS [1,2]*

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At the ***Institute of Animal Biochemistry and Genetics, SAS***, (Ivánka pri Dunaji) the studies of osteodystrophies, egg-shell formation abnormalities, reproductive and adaptive processes in Japanese quail under hypodynamy, hypergravity and microgravity are performed. This project represents a continuation of successful research of Japanese quail embryogenesis in weightlessness aboard the orbital space station MIR. The objective of this project was to obtain the new data on the effect of hypodynamy, hypergravity and microgravity on organism of the quail that could be used in future as a higher heterotrophic link of the autonomous closed ecosystem during a long-term stay of man at orbital and planetary stations.

The method of rearing of Japanese quail chicks under the simulated weightlessness conditions (hypodynamy) from first day after hatching was modified. The adaptability of one-, two- and tree-day-old quail chicks to 2-weeks continuous hypodynamy was studied in three replicates using this method. Because the differences in the results achieved were not found, we have proceeded with an experiment testing the postembryonic development of quail hens in hypodynamy from day 2 to day 56 of age. Differences between the development of hypodynamy reared individuals in comparison with those kept under control conditions were studied by morphological and physiological methods. The obtained knowledge could be applied in study of early postnatal development of Japanese quail under microgravity conditions. Our stationary model of Japanese quail rearing under the simulated weightlessness represents a real alternative to rearing quail in microgravity generated using centrifugation. However, centrifuge of the required size could not be build, because of limited room aboard a space station, in the near future.

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of some tissues and organs of Japanese quail hatched on the orbital space station "MIR". In: *Folia Veterinaria (Supplementum),* 2001, 45, No. 1, S17 - S22.

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The research activities of the ***Institute of Cell and Molecular Biology, Faculty of Sciences, Šafárik University, Košice***, are dealing with observations on the: Accumulation and persistence of cytogenetic damage induced by radiation and other factors of space flight.

The project is based on our preceding studies, in which the accumulation of latent cytogenetic damage in slow proliferating tissues (liver, kidney) in course of continual exposure of animals to ionizing radiation was demonstrated. The aim of this project is to study the possibility of induction and accumulation of the latent damage by other space flight factors in model experiments - hypergravitation, vibration or hypokinesis, for example. From the point of view of long-term space flights, the study of potential possibility of transgenerational transfer of the latent damage to progeny of exposed individuals may be of special importance.

A discussion was started on co-operation with scientists from Institute for Low Temperature Physics of the Ukraine Academy of Science, concerning DNA structure analyses in the exposed individuals and their progeny. The latent damages were studied in the liver of male rats irradiated by gamma rays and their progeny, which manifested itself after stimulation of cell division by partial hepatectomy. After partial hepatectomy, in the regenerating liver of progeny, similar cytogenetic changes (decrease in mitotic activity, increase in chromosomal aberration frequency, etc.) were noted as in that of irradiated fathers but the extent of changes was lower in comparison with the parental generation.

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