Special aspects of the cardiovascular system regulation and cerebral blood flow under gravitational influences. Review (Part I)

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Abstract
The review outlines modern aspects of studying some cardiometic characteristics, the changes of which are associated with ensuring adaptation of central, peripheral hemodynamics, and cerebral blood flow under conditions of an altered gravity vector in the state of weightlessness and its ground-based modeling. The results of studies reflecting the characteristic role of the cardiovascular system and its components are presented: autoregulation of cerebral blood flow, reconfiguration of the regulatory mechanisms of the circulatory system, and starting from the features of myocardial remodeling to changes in large vascular beds. The features of the restructuring of central and peripheral blood flow, microcirculation, as well as manifestations of changes in the reflex regulation of the functions of the cardiopulmonary system in response to gravitational influences, are considered.

Keywords
Weightlessness, Microgravity simulation, Gravitational stress, Cerebral blood flow, Cerebral autoregulation, Cardiovascular reflexes, Cardiovascular system

INTRODUCTION

Over the coming decade, a number of state space agencies of leading spacefaring nations, such as the USA, Russia, Europe, Canada, Japan, India, and China, as well as many commercial space companies, are planning to expand the boundaries of space travel. Space exploration involves great risk associated with both known (ionizing radiation, microgravity) and poorly studied factors (hypomagnetic environment). Thus, there is an urgent need to expand research to determine the limitations of long-term missions, develop crew protection measures, and technological improvements to modern space vehicles for deep space exploration. Researchers are to use innovative technologies, such as artificial intelligence, to expand diagnostic and prognostic capabilities, and to provide high-quality medical care in the space environment [1-4].

With aeronautics advances, some changes are occurring in some modern professions of civilians performing complex activities associated with the need for the body to activate physiological adaptation to space flight and the characteristics of life and activity in a hermetically enclosed volume [5,6]. Further space industry advance is suggested to develop short-time visiting expeditions with a view to reducing the radiation impact on the crew of galactic telescopic rays and solar proton events when flying in polar orbit. Modern orbit injection and descent systems will require faster adaptation of astronauts to weightlessness conditions to carry out competently various operator functions according to the flight program.

Microgravity, in addition to changes in hemodynamic parameters, causes neurosensory irregularities [7]. In particular, most astronauts experience space motion sickness as a form of the vestibulo-vegetative syndrome (motion sickness), in which the astronaut experiences dizziness, headache, nausea, decreased...
appetite, increased salivation, sweating, spatial illusions, etc. This vestibular dysfunction usually manifests itself within 6 days from the start of the flight and then it gradually disappears [8]. Space motion sickness is an important medical and biological problem that greatly affects the astronaut efficiency, in particular the quality of operator activity during the period of his adaptation to weightlessness.

The results obtained in studies of the relationship between functional changes in the human brain and the quality of operator activity at various stages of adaptation to simulated microgravity conditions will be used in developing recommendations for individual prediction of changes in human brain function and operator activity in space flights. One of the most important part of these studies deals with hemodynamic processes at all levels of cardiovascular system functioning, especially the vascular brain supply. Data analysis of cardiovascular system studies shows that under microgravity conditions and in ground-based modeling experiments, in the process of human adaptation to extreme environmental conditions, body’s response manifests itself in changes in the blood circulation characteristics [9].

The role of the cardiovascular system under conditions of earth’s gravity, in weightlessness, and during gravitational unloading

In the process of evolution, the human cardiovascular system has adapted to the conditions of gravity [10-12]. Earth’s gravity activates almost every part of the cardiovascular system (central hemodynamics, peripheral hemodynamics, microvasculature) every time a person stands up [13,14]. When standing and walking upright, gravitational influence redistributes blood from the upper body to the legs and the abdominal region [13,14]. Blood supply to vital organs is ensured by enhancing sympathetic tonic, vasoconstrictor nerve impulses addressed to the muscle vessels of the lower half of the body [15]. At the same time, the vascular resistance of the kidneys, lungs, heart, and brain does not increase [16,17]. The venous return to the heart is reduced and blood accumulates in the veins of the lower extremities subsequently resulting in a loss of the plasma volume in the interstitial space, due to which the cardiac preload becomes lower [11]. The human brain and eyes are located significantly higher than the heart and, therefore, in a standing position disorders occur mainly from the excessive downward displacement of the caudal fluid [11-13]. In healthy people, the provision of cardiovascular reflexes is carried out by specific components and centers of the autonomic nervous system, in particular, this applies to the mechanisms of the arterial baroreflex and cerebral autoregulation, which account for maintaining cerebral blood flow in an upright body position. The changes in the systemic blood pressure range from 60 to 80 mercury pressure; that is, the lower level with physiological hypotension: a decrease in peripheral resistance, cardiac output and contractile function of the heart, which is observed, for example, for highly trained athletes at rest, in people living in hot climates or under conditions of high-altitude hypoxia. An increase in the blood pressure to 160-180 mm Hg occurs during physical activity, gravitational overloads, and similar factors; in this case, the systolic blood pressure can reach 220-240 mm Hg. The cerebral self-regulating mechanisms are capable of maintaining a stable blood supply to the brain without exceeding specific values. In case of insufficient blood supply to the brain (cerebral hypoperfusion), when the systemic arterial pressure drops below 60 mm Hg, i.e., so-called syncope or fainting occurs, which is a temporary, quickly passing loss of consciousness in which a person loses control over his own body and may fall. Such conditions are quite dangerous, since they sometimes arise spontaneously and without obvious precursors, when the mechanisms of systemic and cerebral hemodynamics do not function because of various reasons, including unexpected, sharp psycho-emotional disturbances, and detaining of muscles and blood vessels during a long-term illness with prolonged bed care and microgravity [13,14,18-20]. In addition, the maintenance of posture and systemic circulation is facilitated by the contraction of the skeletal, so-called gravitational muscles (muscle pump), together with the venous valves and the work of the respiratory muscles (respiratory pump), which ensure proper venous return in the upright position [11,20]. Earth’s gravity affects the entire human body and its internal organs, forcing it to maintain a relative tone (increase) of intrathoracic, intracerebral pressure, and peripheral vascular resistance [22,23]. Under conditions of weightlessness or during its simulation, these mechanisms undergo profound adaptive changes. At the altitude of the International Space Station (ISS), a near-Earth orbit of which is about 400 km, all above-mentioned mecha-
nisms should function within the laws of Earth's gravitational field. However, centripetal acceleration counterbalances gravitational influence, so that astronauts and cosmonauts aboard the ISS are in constant free fall (weightlessness). Thus, it is the gravitational effect (or zero gravity – 0g) that is the trigger that forms the process of urgent and long-term adaptation through the involvement of flexible, plastic components of the cardiovascular system at all its levels and the mechanisms of autoregulation of cerebral blood flow to create the final stable allostasis in weightlessness.

A change (decrease in influence) of the gravitational factor causes a serious reconfiguration, first of all, of the regulatory mechanisms of blood circulation as a whole at all its levels, from large arteries to the microcirculatory bed [17, 24-26]. Under microgravity conditions, an outflow of liquid media into the upper sectors of the body takes place. The hydrostatic gradient from the head to the feet is lost, and blood is displaced from the lower extremities and abdominal region to the chest and head [27]. The displacement of fluid to the cranial side results in an increase in the amount of blood in the vessels of the lungs, changes in cerebral blood flow, stagnation of blood in the neck veins, and accumulation of fluid in facial tissues [26]. In contrast to the clinical symptoms that characterize dilatation of the jugular veins as a sign of an increased central venous pressure during space flight, peripheral venous pressure decreases as evidenced by published results [28]. In [29] this was shown using invasive methods. This occurs against the background of an increased or stable cardiac output with a decrease in the systemic vascular resistance in astronauts and with an almost synchronous increase in the activity of the sympathetic division of the autonomic nervous system after staying in a week in space [30-34]. Typically, the increased resting sympathetic nervous system activity is accompanied by vasoconstriction and a decrease in the central blood volume. Therefore, it is paradoxical that the systemic vascular resistance in weightlessness decreases compared to that during the orthostatic test or in a sitting position [35-37], which contradicts the concepts of the influence of the sympathetic nervous system on the vascular tone under gravity conditions [29,38]. Paradoxical facts may also include an increase, under conditions of weightlessness, in the transmural (externally vascular) central venous pressure [23,29]. In a zero-gravity state, a change in the pressure/volume ratio in the veins occurs due to the absence of external pressure (compression) on the organs and tissues of the human body. There is also no pressure on the chest (under Earth conditions it is similar to a constant horizontal position of the body), while the respiratory muscles of the chest relax, the volume of the chest increases due to a change in its shape taking the inspiratory position, which provokes a decrease in the intrathoracic pressure [39,40] below the values of central venous pressure, due to which the transmural filling pressure increases with a subsequent increase in the cardiac output [41]. Koenig [42] and Convertino [43] propose to consider the theory of remodeling of the biomechanics of the heart itself. There has been a report of cardiac distensibility leading to an increase in the ventricular end-diastolic volume and a paradoxical increase in the cardiac output with a decrease in the central venous pressure. The nature of changes in cardiac distensibility is not clear. Presumably, changes in the sympathetic tone play a significant role in this phenomenon.

It is probably worth considering the theoretical background of the anatomical structure of the heart set forth by Torrent-Guasp F. et al. [44]. According to the author, the heart muscle is a double spirally twisted single muscle flap (“tape”) wrapped around itself in a certain way with two main twists with mutually perpendicular directions of muscle fibers: in the base area to the right (clockwise) and in the area apex of the heart to the left (counterclockwise). Accordingly, in the area of the apex of the heart, which resembles a curl, the directions of the subepicardial (outer) and subendocardial (inner) layers change. Between them, there is a middle layer with a circular fiber direction. Taken together, this design is somewhat reminiscent of a difficult tie knot. This orientation of the muscle fibers allows them (during systole, contraction, and coagulation in the base area to the right (clockwise) and left (counterclockwise) of the apical outer muscle layers) to simultaneously act as two pumps: “pump” (bicycle) and “circular” (as in heating or water supply system). The pump creates a pressure in the cavities due to compression: bringing the unfixed apical helix closer to the base of the heart. The circular pump provides a vortex (turbulent) direction of the blood flow into the vessels of the pulmonary and systemic circulation due to twisting. Each contraction looks like wringing out a wet towel with hands. The diastole phase is the same active mechanical process, which, when unwinding, engages the muscle fibers of the in-
ner layers and ensures active blood absorption. Taking into account the fact that there are fewer subepicardial fibers, this process is enhanced due to the involvement of the middle layer of circularly directed fibers of a single muscle “ribbon”. It is interesting that systolic torsion movements change the biomechanical characteristics of the inner layers of the myocardium: the outer layers curl, thicken, and shorten and, in contrast, the inner layers stretch, lengthen, and acquire potential contraction energy. However, not only the anatomical but also the physiological features of this structure of the heart change the idea of the usual time (in milliseconds), periods, and phases of the cardiac cycle. According to this theory, both main phases: systole and diastole are processes of active work, and the duration of the pause or diastasis is negligible. In regard to weightlessness, a cautious assumption can be made that explains the decrease in the systolic function of the heart, which is probably not associated with a lack of load, primarily on the left ventricle of the heart. Due to the absence of the “need” to maintain a constant level of blood pressure in the systemic circulation, at zero gravity, there may be an effect of switching contractile (systolic) function to diastolic (pumping-suction) activity with the involvement of the subendocardial “diastolic” and partially circulatory layers of the myocardium. An option for the development of functional remodeling may be reversible microgravity “diastolic hyperfunction” with a decrease in the mass of the subepicardial layers of the myocardium and the dominance of the “relaxability” function. A hypothetical prerequisite for the development of this effect is also the altered composition of the on-board gas environment with moderate hypercapnia, which could potentially affect the Ca2+ exchange due to an excessive superoxide formation and closure of calcium channels against the background of a possible excess of K ions, which ultimately limits the development of heart rate and contraction strength. It was previously shown that both under conditions of space flight and its simulation of various durations, a decrease in the heart size occurs [45]. In addition, astronauts’ hearts become “rounded”. In just a few weeks under weightless conditions, the heart acquires an oval or even spherical configuration by 9.4% different from the usual elongated shape [46]. During the first 3 days under Earth’s gravity conditions, the heart of astronauts, according to transthoracic ultrasound studies, returns to its original pre-flight forms. [47]. An increase in the cardiac output promotes a change in the hemodynamic flow/volume ratio towards the flow dependence causing a redistribution of the blood volume from the central to peripheral vascular bed [48] and reduces the central venous pressure.

Practically, in weightlessness there is a redistribution of blood from the central vascular bed towards the peripheral one [49]. The increase in the right atrial pressure and central venous pressure should be interpreted as a function of flow, since the central venous pressure falls as the cardiac output increases [50]. In weightlessness, the cardiac output increases from 30 to 40% [37,51,52]. Based on the initial values of the circulating blood volume, it is possible to predict the response of the venous pressure under conditions of weightlessness [37,53] and a possible response to orthostasis [54]: the central venous pressure increases in individuals prone to hypervolemia, but decreases in individuals with hypovolemia.

In addition to changes in the intravascular volume, in a state of weightlessness fluid is redistributed between sectors of the body. The volume of circulating plasma and the volume of extracellular fluid decrease due to the movement of fluid into the intracellular space [55]. The situation may be aggravated by a decrease in the fluid intake due to space motion sickness, which occurs in the early stages of flight, with an increase in the urine output leading to the loss of 1-2 liters of water [55]. In space a decrease in the plasma volume probably contributes to a decrease in circulating natriuretic hormone concentrations [55,56]. These reactions stabilize during the first 2 weeks of stay in space and persist thereafter [55,57]. Unpleasant uncomfortable effects caused by hemodynamic changes during the period of adaptation to weightlessness include congestion of the paranasal sinuses and air cells of the mastoid process [58], nasal congestion [59], and changes in taste sensations [60].

The role of the cardiovascular system reflexes and features of the reflex response to the effects of gravitational stress

Thus, the previous section outlines the main aspects of the structural and functional components of the cardiorespiratory system in the process of adaptation to the conditions of an altered gravity vector. Weightlessness from the initial period of adaptation to 5-6 months of orbital flight initiates processes of reorganization of cardiac activity and myocardial remod-
elung and causes changes in hemodynamics and the manifestation of specific cardiovascular reflexes described by the authors as physiological or pathophysiological processes of the cardiorespiratory system [61,64,70-72,75,76]. The fundamental Frank-Starling mechanism appears describing the "law of the heart or the law of the cardiac fiber" (heterometric regulation of cardiac activity) in which the contractility of the heart increases in response to an increase in the volume of the ventricles. Otto Frank (1865–1944) studied the effect of isovolumic pressure on the heart under experimental conditions (1895) [61]. He discovered an inversely proportional relationship between the degree of stretching of the heart walls (increase in the length of each cardiomyocyte) and the degree of tension and force of myocardial contraction. The pressure-volume curve in the left ventricle shows that an increase in the volume of the cavities of the heart is accompanied by an increase in the pressure in them and an increase in the cardiac output due to an increased contractility of the heart [61]. The English scientist Ernest Henry Starling (1866-1927) in experiments on a denervated heart independently confirmed this law. Changes in this mechanism are confirmed both under conditions of weightlessness, which ultimately leads to a decrease in orthostatic tolerance [62], and in modern experimental models [63].

When exposed to mechanoreceptors located in the area of the right atrium and the mouths of the vena cava with an increased pressure under conditions of the increased venous return to the heart, the "law of heart rate" (Bainbridge reflex) functions. It represents the response activation of the chronotropic function of the heart and is manifested by an increase in the heart rate [64,65]. The manifestation of the Bainbridge reflex should be expected in the first stages of adaptation to gravity-free environment. It is worth recognizing that the well-reproducible Bainbridge reflex (in experimental studies on dogs, to a lesser extent on large primates, and minimally in studies involving humans [66]) gives reason to believe that upright posture is a more significant phylogenetically shaped factor for the development in the human body baroreception due to the role that the arterial baroreflex plays in maintaining posture [67]. This mechanism intensifies at the initial stage of the flight, persists during a short stay in orbit [68], and weakens under conditions of a long flight [69]. Thus, in the initial "acute" stage of adaptation to weightlessness (1-5 days), a positive chronotropic effect (Bainbridge reflex) appears competing with baroreflex regulation. During the transition to long-term adaptation, the mechanism of baroreflex regulation dominates in which the arterial baroreflex and respiratory sinus arrhythmia are maximally synchronized, which emphasizes the active inclusion of parasympathetic regulatory components. In the process of long-term (six-month) adaptation to weightlessness, there is no reafference from the mechanoreception of the support zones of the feet and gravitational muscles. When the involvement of the baroreceptors of the aortic arch and carotid sinuses in the process of controlling systemic blood pressure weakens, baroreflex regulation is inhibited, which leads to the development of orthostatic instability during readaptation to the terrestrial gravitational load. There is one more reflex mechanism worth evaluating. The contribution of the muscle metaboreflex (ergoreflex) to the formation of regulatory responses of the cardiovascular system when performing dynamic (cyclic) exercises to develop endurance with load on the leg muscles has been shown. Under loads of moderate intensity, the ergoreflex is significantly enhanced during space flight. Its strengthening occurs through the activation of the so-called "central command": integrative mechanisms of chemoreception and neurotransmitters are involved, which has a positive effect on the result of baroreflex synchronization with the sinus node. This suggests that the latter can decisively be involved in the regulation of the cardiovascular system in response to dynamic loads under real microgravity conditions [70], the frequency of which should increase towards the end of the flight. Increasing activity of the ergoreflex during physical training in zero gravity is a direct response to neutralizing the existing deficiency of oxygen transport and contributes to an increase in the efficiency of its consumption by working muscles.

The prevailing hypothesis describing the phenomena of hypohydration and associated hypovolemia during flight refers to the manifestation of the Henry-Gauer reflex in which an increased central venous pressure activates receptors in the right atrium of the heart, which send impulses through the vagus nerve to the neurohypophysis. The result is the inhibition of the activity of the antidiuretic hormone (vasopressin) and diuresis [71,72] leading to a decrease in the volume of circulating plasma due to the excretion of fluid by the kidneys and the movement of its part from the vascular bed into the intercellular (interstitial) space.
It is believed that in this way one of the mechanisms for unloading the cardiovascular system is triggered. However, according to the authors [73], in order to stimulate significant diuresis by suppressing the effects of vasopressin, the level of increase in the central venous pressure under microgravity conditions is not enough. Moreover, according to data [71,72], even a slight but persistent increase in the pressure in the right atrium stimulates the release of atrial natriuretic hormone. As a result, the excretion of dissolved sodium in the urine leads to a decrease in the content of dissolved electrolytes in the plasma and interstitial space shifting the balance of the intercellular environment towards hypotonic overhydration. Hypotonic fluid will tend to move into the cellular space forming the preconditions for the development of edema of the head tissue and other water sectors, as well as suppressing water consumption. A dangerous consequence of that is overhydration of brain cells. Thus, the hypothetical negative water balance, which occurs in astronauts under conditions of weightlessness at the stage of urgent adaptation, is formed slowly (2-3 days) as a result of the gradual loss of sodium and water in the urine combined with a decrease in the fluid intake. The formation of an optimal water-electrolyte balance in space flight will ensure more efficient physiological adaptation to weightlessness conditions compared to the conditions of experiments with “dry” immersion, when already on the first day there is a change in body’s water balance manifested by intense diuresis [74].

Finally, the reflex also manifested under conditions of gravitational influences is worthy of attention, which was initially described by A. von Bezold in 1867 [75] and followed by a detailed study of the resulting effects and their description prepared by A. Jarisch [76]. It is currently known as the Bezold-Jarisch reflex and is characterized by a combination of bradycardic and hypotonic reflex responses to chemical (pharmacological) or mechanical stimuli, and the final result of which is vasovagal syncope [77].

The gravitational (orthostatic) load on the tilt-rotary table provokes the outflow of blood to the legs and its deposition in the venous basin of the lower extremities in an average volume of 500 to 700 mL, which leads to an increase in the volume of interstitial fluid, a decrease in the circulating volume of blood, and a delay in venous return to heart causing a decrease in the systemic blood pressure. As a result of a cascade of hemodynamic events, the frequency of impulses coming from low pressure receptors located in the right atrium at the junction of the vena cava and in the left atrium at the mouth of the pulmonary veins decreases, which, in turn, causes activation of the mechanisms of sympathetic and parasympathetic control of the baroreceptor reflex, to maintain the consistency of adequate cerebral perfusion at the proper level of blood pressure under orthostasis conditions. In this case, sympathetic activation causes an increase in the blood pressure and heart rate. However, with an increase in the heart rate and inotropy, the stimulation of the mechanoreceptors of the inferior posterior wall of the left ventricle can cause a parasympathetic response, which triggers pathological bradycardia and hypotension against the background of a decreased vascular resistance. The role of the venous system in this mechanism is not completely clear, although Epstein’s studies in 1968 [79] noted the presence of a high venous tone with a decrease in the blood pressure. Described in 1956 by Sharpey-Schafer E. R. events of a pathological reflex response to the stimulation of mechanoreceptors in the wall of the left ventricle are proposed to be considered as a “ventricular theory” of the syncope development. Moreover, it is orthostatic (gravitational) stress that is the trigger of the “hemodynamic cascade of events” described above leading to the manifestation of the so-called phenomenon of “empty” ventricle. An increase in sympathetic tonic activity, the standard manifestation of which is an increase in the strength of contractions and pulse rate, triggers the Bezold-Jarisch reflex, in which an increase in the sympathetic tone against the background of a sharp loss of filling volume of the ventricles of the heart leads to abnormal reciprocal increasing bradycardia: a drop in the blood pressure instead of moderate postural tachycardia and an increase in the blood pressure.

Full evidence of the paradoxical reflex response to increasing impulses coming from the mechanoreceptors of the left ventricle of the heart against the background of tonic activation of the heart by sympathetic nerves designed to stimulate an increase in the strength and frequency of heart contractions under conditions of low filling pressure of its chambers is presented in the publication [81]. It is noted that the higher the contractile function of the ventricles under contrast drop in their filling pressure, the greater the number of recruited mechanoreceptors and the higher their impulse activity. Under conditions of a paradoxical reaction stimulated by gravitational stress, mechanoreceptors
transmit the flow of impulses along the unmyelinated fibers of the vagus nerve to the stem structures of the medulla oblongata, which allows one to regard the flow of afferent nerve impulses as a state of hypertension on the basis of a combination of patterns. A response decrease in the tonic activity and an increase in the inhibitory activity of the sympathetic vasoconstrictor center are accompanied by a sharp dilation of the arterial vessels and hypotension. At the same time, the cardioinhibitory activation of the dorsal nucleus of the vagus nerve causes a decrease in the heart rate [82].

In [83], when conducting a 5-min orthostatic test at the end of short-term space flights (from 2 to 8 days), the heart rate of orthostatic tolerance astronauts continued to slowly increase. In cosmonauts with symptoms of orthostatic intolerance, a decrease in the pulse rate is detected during orthostatic testing, while presyncopal bradycardia is a prognostic criterion reflecting the pathological activation of the parasympathetic link leading to the activation of the Bezold-Jarisch reflex. Analysis of the results of pre- and post-flight echocardiographic studies of astronauts during short-term orbital missions lasting up to 8 days showed a decrease in both the end-diastolic and end-systolic heart volume when compared with the pre-flight values thus confirming the concept of reducing ventricular preload, which is usually considered as one of the provoking factors causing the Bezold-Jarisch reflex [84].

**SUMMARY AND CONCLUSION**

Thus, having studied the literature data describing the effect of gravitational unloading on the human body using examples of numerous scientific studies in conditions of weightlessness (0g) from short-term 1-2-week to six-month orbital flights and during the transition (readaptation) to earth gravity (from 0g to +1g), the authors come to the following conclusions:

- any changes in the vector of gravitational load affect a person and are reflected by the immediate effect of activation of neurogenic mechanisms of blood circulation regulation;
- the main vital functions of the human body, collectively provided by the complex relationships of the cardiovascular system at all its levels with the overlying “control” centers of regulation and “executive” organs of the circulatory system (heart, great vessels, arterial and venous systems) and autoregulation of cerebral blood flow are linkages of one closed self-regulating gravity-dependent system
- the coordinated work of self-regulation mechanisms allows maintaining gravitational homeostasis and, under conditions of allostatic transitions (space flight and conditions of its simulation; i.e. with a change in the vector of gravitational load on the body), maintaining the required level of brain performance and the main regulatory nerve centers of the medulla oblongata, hypothalamus, and the limbic system, which are involved in maintaining the constancy of the internal environment of the body and affect the functioning of all its systems: cardiovascular, endocrine, digestive, excretory, respiratory, etc.;
- in the process of long-term adaptation to gravitational unloading, the maintenance of physical and cognitive performance occurs due to multilevel functional and structural transformations of the cardiovascular system.

1. Earth’s gravity serves as a constant activation factor for almost every part of the cardiovascular system (central hemodynamics, peripheral hemodynamics, microvasculature) every time a person gets to his feet. A complex system of regulatory hemodynamic processes and reflexively controlled components supporting stable cerebral blood flow ensures verticalization of a person under conditions of +1g gravity. A significant role belongs to highly organized and coordinated mechanisms of the arterial baroreflex and autoregulation of cerebral blood flow.

2. In the absence of gravity, functional and structural adaptive remodeling of the myocardium and arterial vessel walls occurs along with changes in the balance of fluid media and restructuring of the central and peripheral circulation. The mechanism of autoregulation of the cerebral blood flow ensures the constancy of brain perfusion under conditions of gravitational unloading.

3. Under conditions of 0g factor, a cascade of paradoxical hemodynamic changes occurs: an increase (under conditions of weightlessness) in the transmural (externally vascular) central venous pressure, systemic vascular resistance in weightlessness decreases against the background of vasoconstriction, and a decrease in the central blood volume. A change in the pressure/volume ratio in the veins occurs due to the lack of external pressure (compression) on the organs and tissues of the human
body. Blood is redistributed from the central vascular bed to the periphery, the volumes of circulating plasma and extracellular fluid decrease due to the movement of fluid into the intracellular space.

4. The nature and manifestations of intracardiac reflexes change. Reflex mechanisms undergo a number of adaptive changes, in particular, the “terrestrial” mechanism of the arterial baroreflex, under conditions of urgent adaptation to weightlessness and during probably the first 2-3 weeks of the orbital mission, is closely synchronized with cardiopulmonary parasympathetic regulation, but subsequently, the baroreflex sensitivity is lost by 5-6 months. The restoration of the baroreflex function is facilitated by the physical activity aimed at developing the qualities of endurance in the leg muscles. Such loads have a modulating effect on the baroreceptor activity and form stable regulatory patterns: an increase in the frequency and power of impulse discharges in the vasomotor center of the medulla oblongata is synchronized with the work of the heart and afferent impulses from baroreceptors, which, in turn, ensures the maintenance of the sympathetic tone of muscle vessels at the proper level. The control mechanism for assessing the efficiency of preventive measures is the activation of the muscle metaboreflex (ergoreflex), which indirectly reflects the restoration and stabilization of the process of baroreflex regulation of blood circulation.

5. Diagnostic and prognostic factors include the manifestations of reflexes recorded under conditions of orthostatic testing and short-term modeling of microgravity and hypogravity effects on the human body. In particular, both intracardiac and extracardiac mechanisms that form the reflex response usually have early predictors, the timely assessment of which allows one to avoid complications, for example, presyncope and vasovagal syncope, in the selection of candidates for participation in experimental studies with an altered gravity vector and promising participants in space flights.

FUNDING

The material was prepared as a part of the research work on the topic “Structural and functional changes in the human brain and their impact on operator activity at various periods of adaptation to the conditions of simulated microgravity” (code “Cerebrum-A”) of the state task of the Federal State Budgetary Institution “FNKTs KM” FMBA of Russia for 2023 and for the planning periods of 2024 and 2025.

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