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Gravity and the Tonic Postural Motor System

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Abstract—Inesa Benediktovna Kozlovskaya is the head of a branch of the Institute of Biomedical Problems of the Russian Academy of Sciences, Doctor of Medical Sciences, Professor, Corresponding Member of the Russian Academy of Sciences, Honored Scientist and Engineer of the Russian Federation, a specialist in gravitational physiology, a participant in biomedical investigations during the spaceflights of the orbital stations Salyut-7, Mir, and ISS, as well as the flights of Bion biosatellites. She is one of the developers of the system of counter measures against unfavorable changes in the body in manned flights. She founded the school of the gravitational physiology of movements. Her scientific achievements are awarded with Russian and international prizes and awards. The editorial board of the journal sincerely congratulates Prof. Kozlovskaya on her ninetieth birthday and wishes her well-doing and many more years of active life.

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Spaceflights (SF) are invariably associated with changes in the sensorimotor functions. Interfering with the activity of the main proprioceptive systems, primarily the vestibular and locomotor systems, weightlessness creates conditions for transformations in the systems of motor control manifested by reorientation of the motion control systems to more reliable ones under new conditions system (mainly vision) and by changes in the tactics and coordination structure of movements and the character of motor synergies. These changes, adaptive in their essence, determine the secondary development of a number of unfavorable symptoms comprising the patterns of the syndromes of space motion sickness, microgravitational ataxia, and muscle detraining that impairs the motor possibilities and work capacity of cosmonauts in the course of the flight and, especially, after long-term SF [1–3].

Since the era of SF, Russian scientists have been conducting the studies of the basic mechanisms of intersensory interactions and the activity of movement control systems under the ever changing gravitational environment. With the development of the practice of long-term space expeditions, these studies are being conducted in a complex manner, in the framework of goal-oriented programs, and include human in-flight and simulation experiments, pre- and postflight examination of space crews, as well as complicated in-flight and ground-based animal experiments.

The main tasks of these investigations are as follows:

1. To quantitatively describe the specific features of performance of movements different in the organization of control, composition, regulated parameters, the effectors, and the degree of complexity under microgravity conditions;

2. To determine the quantitative characteristics of the physiological systems and mechanisms involved in the formation and realization of movements, the proprioceptive systems: vestibular, locomotor, muscular; the motor apparatus; and basic reflex mechanisms under the same conditions;

3. To reveal the factors and the main trigger mechanisms in the development of motor disorders under microgravity conditions in order to determine possible methods for their prevention, on the one hand, and

the place and role of the gravitational factor in the activity of various motor mechanisms, on the other hand.

The ground part of the study programs was mainly carried out by research workers from the Institute of Biomedical Problems (IBMP) in collaboration with the representatives of academic institutes and universities; the flight part was, as a rule, implemented under the framework of close international cooperation. Specialists from ten countries took part in the experiments on the Mir orbital station (OS). Cooperation projects were of complex character and constituted an inalienable part of the Russian national program. For example, in the Mir–Shuttle and Mir–NASA projects implemented for a number of years (1993–1997), the sensorimotor investigations section included fifteen experiments studying the effect of weightlessness on different structures and mechanisms of the motor system: muscles, the vestibular apparatus, the spinal reflex mechanisms, posture- and locomotion-regulating mechanisms, etc. Nine of them were developed jointly by Russian and American specialists [4]. In the RLF (Russian Long-Term Flight) project carried out in the course of a 14-month flight of the space physician V.V. Polyakov with the participation of seven crew members in three long-term space missions, four large programs realized jointly by Russian and Austrian scientists and naturally complementing the above-mentioned Russian–American projects that also were devoted to sensory motor investigations [5–9]. The complexity of these projects, their clear orientation and complementarity, a relatively large representativeness of the sample, and the high technological potentialities provided for the possibilities of the acquisition of novel unique data expanding modern ideas of the mechanisms of the effect of weightlessness on the musculoskeletal system.

The Features of the Performance of Differently Organized Movements in Weightlessness

The program of investigation of the kinematic, temporal, and precision characteristics of voluntary movements differing in organization (programmed or tracking), composition (eye, head, and arm movements), modality of controlling sensory signals (vision, hearing, proprioception), and regulated parameters (position, velocity, effort) was implemented during SF in the framework of the experimental Russian–Austrian Monimir project [6, 8, 9] and the Russian–Bulgarian Shipka experiment [10]. In the former, the studies were conducted with the participation of nine members of long-term space missions; in the latter, with the participation of four cosmonauts. The results of these experiments complemented with the data of similar investigations carried out on twelve rhesus monkeys during 7- to 14-day Bion flights [11–15], as well as the data on numerous ground-based experiments with simulation of microgravity conditions (immersion, suspension, antiorthostatic hypokinesia), showed ataxia to be a natural consequence of gravitational unloading. In all the above situations, marked disorders of precision control of the predetermined movement parameters were noted. For example, under dry immersion (DI) conditions, the error values and the reproduction variability considerably increased when a simple motor task of maintaining a certain level of effort was performed [16]. The same results were obtained when the task of maintaining the electromyographic activity of lower leg muscles corresponding to this effort was performed as well as when "isotonic" movements at the ankle joint were reproduced [17].

A sharp minimization of the possibilities of precision control was revealed more clearly when the muscle effort gradation test was performed in the course of which the investigator made a series of sequentially increasing (or sequentially decreasing) efforts from the minimal (the scale absolute threshold) to the maximal one with minimum difference between the neighboring efforts (the differential threshold) [18]. In weightlessness, as well as during immersion, the number of distinguishable gradations was drastically reduced, and the absolute and differential threshold values were considerably increased. These changes persisted after long-term SF for 3–5 and more days. An activation of visual feedback increased task performance precision; however, ataxia-inherent changes in the structure of the tasks set were markedly pronounced; i.e., they lost the pattern of a quick and smooth approach to the target acquiring the character of slow intermittent movements approximating distance to the target.

Still more marked were the changes determined by real and/or simulated weightlessness in the characteristics of motor responses such as the gaze fixation reaction [19–21], postural corrective responses [3, 22], etc. The investigation of the effects of weightlessness on the mechanisms of posture and locomotion regulation were performed under the framework of pre- and postflight check-ups of spaceship crew members, as well as under terrestrial simulation experiments with immersion and hypokinesia of different duration [18, 23–25]. Only in one joint Posture experiment performed by Russian and French astronaut researchers, the mechanisms of regulation of postural activity were investigated in-flight [26].

The tasks of investigation of posture in ground-based simulation experiments were to reveal the main factors determining the development of disorders and the mechanisms of their action (changes in the function of the sensory systems and the associated disorders of the body scheme, changes in the state of basic reflex mechanisms and the muscular system) as well as to study the role and the forms of involvement of gravity in the regulation of vertical posture and locomotions [22, 27]. The results of investigations, having confirmed the idea of the multifunctional nature of disturbances of these functions in weightlessness, led us to the conclusion that the mechanisms of these disorders substantially differed at different stages of exposure to gravity. The studies showed that changing over to weightlessness was accompanied in astronauts by facilitation of vestibular reactions and their decreased static and increased dynamic excitability [11, 28, 29]. Further, in the process of adaptation, vestibular excitability decreases; the vestibular canal is largely excluded from the system of sensory support of movements. Note that the role of afferent afferentation in the systems of motor control substantially increases [30].

The validity of these conclusions was confirmed, in large measure, by the results of the investigations of the effects of weightlessness on the characteristics of complexly coordinated head and eye movements ensuring quick and precise gaze fixation on the object projected in the retinal peripheral field [6, 19, 21]. The latter were performed in SF with the participation of the crew members of short-term (7 days, 19 cosmonauts) and long-duration months-long (29 cosmonauts) space expeditions [19–21], as well as on 12 rhesus monkeys in the flights of Kosmos biosatellites [11]. Marked facilitation of vestibular responses to semicircular canal and otolith irritations manifested by a sharp increase of the vestibuloocular reflex coefficient (CVOr) and a significant increase of neuronal responses of vestibular nuclei and vestibulocerebellum to adequate vestibular stimulation were revealed in all the animals during the first 24 h of the flight. At day 5–10 of the SF, the redundancy of vestibulooculomotor transfer and the intensity of neuronal responses of the vestibular nuclei gradually decreased (with the preservation of high neuronal activity in the vestibulocerebellum): by the end of the flight, CVOr in eight monkeys was close to 1 [11]. Close CVOr values, although exceeding 1, were recorded after SF in 70% of cosmonauts, participants in short-term expeditions. After long-term flights, the CVOr value in a large number of cosmonauts (25%) was sharply decreased; in three cosmonauts up to 0. This decrease significantly disturbing the conjugate activity of the head and eyes persisted after long-duration flights for no less than four days and longer.

Muscle Tone, Spinal Reflex Mechanisms: Postflight Examination Data

The mechanisms of a sharp decline in the strength-velocity qualities of skeletal muscles during transition to weightlessness and their similarly quick recovery on return to terrestrial gravity conditions have long been addressed. Some data for understanding this phenomenon were obtained in the works of Kakurin et al. who suggested its secondary reflex origin and investigated in this context some other characteristics of the state of the neuromuscular apparatus, namely, the tone of muscles and their reflex excitability [23, 31].

The authors assessed the muscle tone by the cross stiffness parameters using two techniques available at that time: those of Czirmai and Ufland [23]. The quantitative relationship between muscle tone and its transverse (or longitudinal) stiffness is a subject of discussions; however, there is no doubt that this ratio for each given muscle under the same standard conditions is constant enough, which is evidenced by many clinical data. The state of the reflex mechanisms was judged by the parameters of the electromyographic patellar tendon stretch reflex evoked by a strain-gauge hammer recording the strength of mechanical stimuli.

In the first investigations performed with use of Czirmai tonometer 24 h after completion of a two-day (two cosmonauts), three-day (two cosmonauts), and four-day (one cosmonaut) flights [23], all the cosmonauts showed a significant decrease in the cross stiffness of m. quadriceps femoris and, to a lesser degree, m. tibialis anterior. Note that the stiffness of m. biceps brachii did not change. The degree of stiffness modulations did not reveal a relationship with flight duration: the highest decrease values of the muscle stiffness were observed in cosmonauts staying in weightlessness 48 h; the lowest values after a 95-h flight.

The studies of the characteristics of the tendon (patellar) reflex conducted in 15 Soyuz crew members launched into space on a two-, three-, four-days, and longer mission revealed in all those examined (except two) a clearly seen increase in the reflex electromyographic amplitude.

Analysis of the literature of the 1970s led us to the conclusion that both phenomena—extensor atony and tendon hyperreflexia—are developed in weightlessness as a direct immediate response to reduction of gravitational loads. It was shown that one of the immediate responses recorded in humans in transition to weightlessness is a postural flexor position indicating a decrease in the activity of lower leg extensors affording the maintenance of an upright posture on earth. Indications of well-defined extensor hypotension also contained the results of neurological examination performed immediately on completion of flights of several hours duration [23].

In manned and animal flights along the parabolic trajectory (a Kepler orbit), depression of the electromyogram (EMG) of lower leg extensors and facilitation of that of flexors was recorded in the weightlessness phase [32]. Bioelectrical silence of the extensors was retained throughout the microgravity phase being replaced by hyperactivity in the G-load phase. The same also held for the phenomenon of hyperreflexia noted during the first postflight medical check-ups [31]. An increase in the tendon reflex response amplitude was noted by the American authors in the Skylab crew members; however, the characteristic chosen for the quantitative analysis of changes, namely, the duration of reflex response varied ambiguously in the course of the expeditions owing to which no conventional quantitative data were obtained [33].

In the 1980s, the described phenomena were again the subject of in-depth studies. The following tasks were set: (a) the quantitative assessment of developing in-flight changes; (b) the time course of their development in flight and in the readaptation period; and (c) their role in the development of hypogravitational disorders of the locomotor system. In order to increase the correctness and accuracy of the results obtained, the research methods employed in the experiments were updated and improved [34]. For example, a new, highly sensitive myotonometer was developed for muscle stiffness quantification, which allowed the transducer application force and tissue response to be independently and objectively measured in a wide range of application forces [34]. Rigorous standardization including the uniformity of transducer application forces in the range reflecting the properties of the underlying muscles, reproducibility of the position of the test link, and control of the level of muscle relaxation and tension with an electromyographic feedback signal ensured the accuracy of the results and the reliability of the method.

The results of investigations performed with the participation of six cosmonauts using this method revealed on Day 2 (more than 48 h) after completion of a 7-day SF a 15 and 20% decrease in the transverse stiffness of m. triceps surae (the gastrocnemius medial head and the soleus muscle, respectively) [34, 35]. Comparing these data, we can maintain that stiffness modulations in the first hours after return from zero gravity conditions were substantially more profound.

After long-term flights, ankle extensor atony in most cases attained the level of pathology: muscle tone was completely lost; when the leg was raised, the muscle assumed the shape of a drop, which was only partially corrected on maximum voluntary contraction [35]. The depth and duration of reversal of tonic disorders in the crew members of long-term missions into space substantially differed without revealing a close dependence on flight duration. The tone recovery curve was clearly two-phase with a relatively abrupt increase over the first two to five postflight days and the gradual slow approximation to the baseline state in the subsequent 7–11 days. No objective instrumental investigations of muscle tone in the course of long-duration flights were carried out.

The state of the systems of locomotor and muscle afferentation on completion of space expeditions was determined for the former by the vibrosensitivity thresholds at 63, 125, and 250 Hz of the main support zones on the heels, in the middle of the support (external) foot arch, under the big and the fifth toe and on the big toe ball [2] where an especially high density of vibration-sensitive Vater–Pacini corpuscles responsive to support loads is observed and for the latter by the characteristics of the tendon reflex involvement curve—by the involvement threshold and the peak electromyographic response amplitude, which is a stimulus strength function. According to the data of Kozlovskaya et al. and despite the generally accepted opinion, these parameters are not interrelated and reflect the properties of different elements of the motoneuronal constellation, namely, low-threshold (threshold) and high-threshold (the peak amplitude) motoneurons. The comparison of the involvement curve characteristics at rest and during performance of the task of retaining the position of dorsal or plantar flexion with the contralateral leg allowed the investigation of the state of the mechanisms of cross synergies—an important element of the organization of locomotor activity [1, 2].

In the first studies conducted in the crew members of the second and third missions on Salyut-6 orbital station, it was found that long-term stay in weightlessness was accompanied by a considerable decrease in the thresholds of vibrosensitivity of foot support zones [1, 36]. The tendency for the thresholds to decrease was later confirmed in a large number of short- (8 of 9) and long-term (5 of 7) space flight participants [1, 2, 37]. The decrease depth in short-duration flight crew members varied within an average of 50% of the background values and was 75% and higher in long-term space flight participants. The most marked and persistent were changes in the thresholds of responses to stimuli at a frequency of 63 and 125 Hz, which are close to the frequency range of sensitivity of Vater–Pacini corpuscles. For example, after a 140-day SF, increased vibrosensitivity in the range of the above-mentioned frequencies was retained in the crew members for at least 42 days. On the contrary, in two short-term and in two long-term space flight participants, postflight vibrosensitivity of the foot support zones decreased. We cannot help pointing out that one of the crew members in short-duration SF was an astronaut from the Republic of Cuba who used, in compliance with the experimental conditions, a Cupula Sand device exerting mechanical pressure on foot and artificially simulating support zones of soles [36]; the other participant of this long-term space flight was a Russian cosmonaut who was the first to use in the course of the spaceflight the bare foot running [2].

As mentioned above, the assessment of the state of muscle input and the related mechanisms of spinal regulations was based on determining the parameters of the curve of the tendon reflex of the lateral gastrocnemius muscle (Achilles, T-reflex). The test choice was determined by its simplicity and information value: human tendon reflexes are well-studied; multiple investigations have proved their monosynaptic nature and a close connection with the system of muscle reception. To construct the curve, we tapped on the Achilles tendon with different strength varying between the threshold and maximum strength using a strain-gauge hammer.

The studies conducted in the crew members of long-term space flights on Salyut and Mir OS, as well as in short-duration SF participants [2, 38–40], showed that a regular effect of both short- and long-term stay in weightlessness is hyperreflexia showed up by a sharp decrease of the reflex thresholds. After 140–185-day flights on Salyut-6 OS, the T-reflex thresholds, instead of the initial 1000 g and more, decreased to 500 g (SE-3), 300 g (BI), 200 g (SE-2) and more [1, 2]. In many cases, we failed to determine the threshold value as the lightest tap on the tendon was accompanied by the appearance of the reflex EMG. In many cases the extension of the reflex receptive field was observed, and (e.g., in SE-2), the clonic activity was recorded: in response to one tap, two or three EMG bursts spaced apart by 150- to 180-ms intervals, occurred.

As distinct from the usual states of hyperactivity of the reflex mechanisms, the threshold decrease in all crew members on the Salyut-6 orbital station was not infrequently accompanied by a decrease in the reflex amplitude and the gradient of its increase [2]. These changes persisted after the flight much longer than changes in the thresholds revealing the tendency to recover as early as postflight Days 5–6. The mechanisms of interlimb reflex interactions were significantly impaired postflight: voluntary stretching of the contralateral leg gastrocnemius muscle on maximum dorsiflexion at the ankle causing preflight reflex repression did not influence its parameters after the flight.

The subsequent studies that significantly expanded the experimental facilities and increased the number of observations confirmed, on the whole, the consistent character of directionality of the main changes in the T-reflex parameters but, nevertheless, revealed the ambiguity and variability of one of them, namely, the maximal reflex amplitude. For example, it appeared that after a flight of one year duration, the maximal T-reflex amplitudes in both crew members truly surpassed the preflight values; the excessive reflex amplitude was retained for seven–nine days. A similar directionality of changes was noted when the crew members of the fourth prime expedition on the orbital station Mir were under observation, in whom on Day 6 after completion of the flight of 151 days duration for two cosmonauts and 241 days for one cosmonaut a marked (2.5–3-fold) increase in the maximal response amplitude was noted along with a marked decrease in the reflex thresholds and inhibition of activity [38, 39]. The presence of obvious and significant changes of different directionality after long-term flights indicated a possibility of the existence of the complex of factors determining, in the final analysis, the studied characteristic. The following could be attributed to these factors: (a) like the initial (background) reflex amplitude and the activity of the cosmonaut that was changed uncontrollably on the preflight examination day; (b) the state of the muscle apparatus (i.e., the markedness or, vice versa, nonmarkedness of atrophy), which, in turn, is determined by the level and type of preventive measures used by the cosmonaut in flight; (c) the cosmonaut's postflight mode of activity; and other factors.

In conclusion, it can be said that staying under real weightlessness conditions is accompanied by the signs of hyperreactivity in the system of tendon reflexes manifested by a substantial decrease in the thresholds of Achilles and patellar reflex (after the flights of any duration), as well as by its amplitude increase. However, the changes in the latter characteristic of the crew members of long-term expeditions varied considerably after the flight, revealing negative dynamics in a large number of cases.

Results of the Studies Performed in the Course of SF

In connection with the foregoing, we think it important to systematically investigate the state of spinal reflex systems throughout the SF. Such investigations were carried out in the late 1980s–the early 1990s on the OS Mir by Russian and Austrian physiologists with the participation of one Austrian astronaut whose duration of the flight was seven days and nine Russian cosmonauts whose flight duration varied between 125 and 429 days [6]. The electromyographic and kinematic parameters of the patellar reflex were studied using a specially designed apparatus, which consisted of the support providing the standard position of the test limb with the subject lying in a supine position, and a mechanical device reproducing by means of a spring the blows of three standard intensities on the patellar tendon. The strength of blow was determined by spring tension when the impact device was deflected by 14, 28, and 42 angular degrees. The enhancement and recording system DataMir used for a number of Russian–Austrian experiments provided the correct recording of the electromyographic components of response. The motor component was recorded by means of the stereo video analysis system. Since changes in the amplitudes and the duration of evoked reflex movements in weightlessness were largely determined by the features of the biomechanics of movements, much attention in analyzing the results was paid to the electromyographic response recorded by surface electrodes in m. rectus femoris.

The results of the studies supported the suggestion that tendon reflexes, in particular, the patellar reflexes, are facilitated under microgravity conditions. This was primarily evidenced by the fact that, in weightlessness in the first days of the flight, a single well-organized, more often dual-wave electromyographic response to a single impulse characteristic of earth was replaced by a polyphasic response with markedly pronounced clonic packs. As a result, the duration of response to a single impulse increased from on minimum 50–80 to 500–2000 ms and more

Table 1. Factors mediating the action of weightlessness on the motor system in real SF and ground-based microgravity simulation experiments

Simulations	Operating factors			
	mechanical load	support reaction	range of movements	vestibular function
Spaceflight	Absent	Absent	Slightly decreased	Disturbed
Antiorthostatic hypokinesia	Decreased	Redistributed from feet to the body surface	Considerably decreased	Intact
Dry immersion	Decreased	Eliminated	Considerably decreased	Intact
Suspension	Decreased	Decreased or absent	Preserved	Intact

on maximum stimulation [7]. In the latter case, the primary stimulation time increased twofold.

The response amplitude in the first days of the flight revealed a tendency to decrease. Varying in cosmonaut V-ov on stimuli of different strength between the preflight 1.2 and 3.6 mV, it decreased to 0.8–2.8 mV on Day 30 of the flight. The maximal response amplitude also modulated in a similar way in a seven-day flight of the Austrian cosmonaut whose preflight involvement curve at predetermined stimulus strength was in the 0.4- to 1.2-mV range, clearly decreased inflight to 0.3–0.8 mV, and sharply increased to 2, 3, and even 4 mV at four to five postflight days.

However, during long-duration flights, the regularity of changes in the electromyographic reflex amplitude appeared to be different. After the primary decline in the first month of stay in weightlessness, the response amplitude in two Russian cosmonauts increased attaining 8–9 mV and more at 60 days of the flight. These maximal amplitude response values remained after the flight as well. A distinctive feature of the involvement function in long-term flights was also its abrupt increase and clear instability showing up in lesser markedness of the relationship between the response amplitude and stimulus strength. While the preflight and postflight response value to maximum stimulus exceeded that to minimum stimulation by 50–200% (preflight and in the first days after completion of a month-long flight), this excess in the period of inflight sharp reflex facilitation could attain 600–700%, supporting the idea of the involvement of most elements of the motoneuronal reflex pool in response.

One of the integral parameters of the states of the postural tonic control systems is physiological tremor (PT) accompanying under terrestrial gravitational conditions all types of activity connected with the maintenance of the position of the body or its parts in the gravitational field of Earth. Although the genesis of PT and its high-frequency component (8–12 Hz) remains the subject of discussion, its close link to the mechanisms of the stretch reflex and the function of muscle spindles appears to be obvious. In this context, being interested in unraveling different aspects of the influence of weightlessness on the mechanisms of motor regulation in parallel and in close connection with the investigations of reflex spinal mechanisms, Russian and Austrian investigators studied jointly in the same experiments and in the same cohort the characteristics of PT of arm at rest and during performance of the outstretched (forward) arm positioning tasks at rest and at low levels of loading [9]. As shown by the investigations, transition to weightlessness determined virtually complete disappearance of the high-frequency (8–12 Hz) PT component in all the ten participants in the space experiment. High-frequency silence occurred immediately in transition to microgravity conditions and persisted throughout the flight no matter how long it could be. Simultaneously, inflight recordings revealed the presence of regular low-frequency (3–5 Hz) tremor that increased with the duration of the flights. Since the earlier special investigations showed that resonance frequencies for relaxed arm constituted 2 Hz for humans [9], these oscillations were not a passive reflection of mechanical oscillations of the body–arm system and could be of regulatory nature.

Simultaneous change in the master frequencies in the work of the control systems in transition to microgravity directly indicated a change in the head (levels) of regulation, as well as more indirectly, the presence of the trigger factor affording the choice of one system under 1 G conditions and the other system, under 0 G conditions. The validity of this suggestion was confirmed by immediate restoration of the PT high-frequency component, which was sharply increased in the first postflight days in all test situations and all movements of cosmonauts after landing on earth after being in space.

As indicated earlier, PT at a frequency of 8–12 Hz recorded preflight during investigations on the stabiloplatform in only 20–40% of the examination time and mainly during a complicated stance, after the flight occupied 100% of the observation interval in both convenient and loading posture. In the EMG of lower leg muscles, m. tibialis anterior and m. gastrocnemius, the rhythmic group activity at the same frequency never revealed preflight corresponded to these oscillations. The markedness of tremor and the duration of its excessive characteristics correlated, in certain measure, to the duration of the flight.

Considering the total data on the neurophysiological studies, it may be suggested that all three phenomena revealed in the course of their performance are interrelated and are determined in transition to weightlessness by a unified factor, namely, deactivation (or a sharp activity decrease) of the system of tonic muscle control. The pattern of exclusion (or lesser participation) of tonic antigravitational muscle fibers from muscle activity inevitably includes atony, a decrease in the absolute strength of muscles as a function of the number of fibers this muscle contains—a decrease in the density of proprioceptive flow, which contributes to the development of the signs of partial deafferentation, including hypersensitivity and hyperreflexias, and, finally, the disappearance of postural tremor mainly reflecting the activity of tonic mechanisms. A trigger for deactivation of the tonic system in weightlessness and its reactivation on return to 1 G conditions may be the gravireceptor systems, primarily otolithic and support afferentations specially oriented to reception and analysis of gravitational loads and rigidly built in the mechanisms of organization of postural synergies.

Terrestrial Hypogravitational Models

As indicated in the introduction, an important contribution to the development of modern notions (knowledge) of the nature of the influences of microgravity on the sensorimotor functions was made by systematic terrestrial simulation investigations, in which the factors occurring in weightlessness, namely, decreased level of muscle activity, workload reduction, lesser changes in the activity of different afferent systems, were studied systematically and differentially (Table 1) [37].

Immersion

Immersion (exposure of a test pilot to a liquid medium) seems to be the most promising model for studying hypogravitational effects in humans. A similarity of immersion to weightlessness was evident even to Tsiolkovsky who wrote the following without detailed scientific analysis of similarity between the factors of the two conditions: "After an explosion, the weight must disappear. The traveler will feel like a duck to water." The support-free environment and the loss of weight load, which postulate a similarity of biomechanical principles of motor activity in immersion to those in weightlessness at first determined the choice of immersion as the only model for training and teaching cosmonauts the motor habits and operations in weightlessness. However, as far back as the early 1960s, researchers investigating the physiological effects of immersion for its possible use to simulate the effects of weightlessness on earth [11, 41] discovered two factors determining the discomfort and possible harmfulness of long-term exposure of skin to water, which restricted these possibilities. Considering these factors, Russian investigators developed the dry immersion (DI) model whose conditions allowed the body to be separated from water by an elastic, waterproof free floating cloth [42]. Since then, immersion has become a leading model in the studies of simulation of 5–7-day exposures to microgravity (the duration equal to that of short-term guest space expeditions) in Russia. However, in separate experiments, the possibility of safe prolongation of DI to 56-days was shown [43].

In the course of conventional investigations with dry immersion, test pilots are immersed in a horizontal position into a 200 × 100 × 100 cm bath filled with water whose temperature was maintained within 33 ± 0.5°C. They are isolated from contact with water by a free-floating cloth. The day regimen during immersion includes the time for the performance of experimental procedures, hygienic operations, and prophylactic measures. Test pilots are removed from the bath twice daily and placed on a trolley in a strictly horizontal position for administering hygienic procedures. On the whole, such effects of weightlessness as hypodynamia, elimination of the vertical vascular gradient, removal of mass load and, accordingly, support stimuli are completely reproduced in immersion.

Head-Down-Tilt Bed Rest

Since the mid-1960s, head-down-tilt bed rest (HDBR) with an angle of 6°–8° proposed and developed by a team of researchers from the laboratory headed by L. I. Kakurin has occupied a leading place in the experiments designed to look into long-term effects of weightlessness [44]. From the point of view of physics, this model also reproduces all the above-mentioned characteristics of weightlessness: namely, hypodynamia, hypokinesia, decreased static and dynamic muscle loading, redistribution of bodily fluids cephalad, and elimination of weight loads from the main sensory areas of weight sensitivity, which are the feet in humans and mammals. As shown earlier, long-term head-down tilt also reproduces quite accurately the effects of long-duration SF in all physiological systems, including the cardiovascular, the cardiorespiratory, the skeletomuscular, and the motor control system [44, 45]. In further investigations, HDBR was also widely used to determine approaches to the development of prophylactic agents for the unfavorable effects of long-term SF on the human body and to the experimental assessment of the efficacy and safety of the prophylactic remedies proposed for flight.

Suspension

Suspension, a model developed in Italy and Russia in connection with the planned flights to the moon, is of special interest to researchers working in the field of motor control [46]. The model opened the possibilities of studying the kinematics of various movements in unloading or balancing all parts of the body. Later, the modified model of suspension was and is being used in animal experiments [47–49].

Changes in the Sensorimotor Functions under Simulated Microgravity Conditions

The results of the physiological investigations carried out in the spaceflights allowed to suggest that after staying in a weightless environment, sensorimotor functional disorders are in large measure determined by deactivation or a substantial decrease in the activity of tonic control mechanisms determined, in turn, by changes in the activity of gravitational sensory inputs. Testing and the development of this hypothesis were the main goal of a considerable number of ground investigations performed at the Institute of Biomedical Problems by a large group of researchers using the two hypogravity models, namely, DI and HDBR.

The research was focused on studying the state of the mechanisms of motor control and sensory functions—the muscle tone, the activity of motor units in the course of voluntary motor test performance, as well as spinal reflex mechanisms, under simulated microgravity conditions.

Muscle Tone

As shown earlier, the development of regular response to transition to weightlessness is a flexor attitude. In the 1970s, when the work connected with the preparation of flight missions to the moon where the gravitational level constitutes one-sixth of the terrestrial level, the experiments designed to study the biomechanical and kinematic characteristics of locomotor responses under these conditions were simultaneously carried out in Italy and in Russia [46]. To reduce gravitational load, both groups of investigators used the model of hanging all segments of the human body. The investigations convincingly showed that reduction of gravitational loads and the associated weight loss and support loads were accompanied by the development of the flexor posture whose markedness is directly proportionate to weight unloading. Similar results were also obtained in monkeys [47]. These data led us to suggest that support afferentation is the main factor in the mammalian motor system signaling the brain the needed degree of deactivation of the antigravity posture system.

The tone of muscles controlling the movements of the ankle was investigated under conditions of a number of simulation situations differing in the degree of support unloading, namely: (a) under DI conditions when the weight is equally distributed across the body surface, thus excluding the appearance of the support gradient in any part of the body; (b) under HDBR conditions where the support loads are preserved but redistributed in large areas of the back and the lateral aspects of the body not connecter with the maintenance of the upright vertical posture; and (c) under complex conditions in which the test pilots were in the daytime (12 h) under DI conditions; and at night (12 h), under HDBR conditions. Tone modulations were investigated using the means and methods described above.

Fifteen test pilots participated in the experiments; the duration of DI and complex session were seven days; of HDBR, 14, 30, and 120 days.

The results of investigations showed that staying under the three simulations conditions was accompanied by significant alterations of the stiffness of the three heads of m. triceps surae: the lateral and medial heads of m. gastrocnemius and m. soleus. The dynamics and the degree of changes under different conditions varied considerably [17, 18, 34]. In DI, the development of the transverse stiffness reduction occurred exceptionally quickly attaining the maximum reduction level of 40–50% of the initial level at six hours of exposure. Under HDBR conditions, the stiffness alterations appeared at a much slower rate; the reduction time in this case measured in days, but not in hours as in DI. Accordingly, the maximum reduction level constituting 60–70% of the initial one was attained at the interval between Day 14 and Day 31. Finally, under the conditions of complex DI and HDBR influence, the depth and velocity of alteration development were lesser than in DI but greater than in HDBR. In m. tibialis anterior, the transverse stiffness reduction under immersion and HDBR occurred much later and did not attain 10–15%.

After seven days of DI, the stiffness reduction in the first 1–3 days after completion of exposure to microgravitation was 25–30%; after seven days of SF, 15–20%; after HDBR, 10–15%. The degree of changes in the stiffness of muscles during their maximum voluntary contraction was distributed in the same way as in muscles at rest.

Motor Units: The Order of Involvement

A considerable contribution to understanding the nature of the processes induced by gravitational load reduction was made by the results of investigations of the order of involvement of motor units (MU) in performing the small effort retention task (about 10% of maximum effort) for 60 s. The studies were conducted under seven-day DI and 120-day HDBR [2, 16, 50].

In DI, the test pilots were able to perform the motor task; however, the analysis of MU activity revealed substantial changes in its characteristics, which were most markedly pronounced at three days of exposure [16]. The average duration of interspike intervals in DI increased, which was resulted to an increase the number of high amplitude and low frequency MU in the histogram.

Before the DI onset, the number of MU with an average interspike interval not exceeding 170 ms was about 85%. Under DI conditions, it decreased to 60% and the number of MU with an interspike period (IPP) of 190–230 ms increased from 35 to 60% accordingly. Simultaneously, IPP variability was considerably increased: the standard deviation value equal to 16 ms before exposure increased to 26 ms. Comparative analysis of changes in the slope of the regression curve describing the relationships between the standard deviation and the IPP time gave evidence of the IPP variability increasing at a faster rate than IPP duration. On the whole, MU changes indicated that the small effort retention task under DI conditions was performed by a different motor unit population rather than the control one and that the activity in the system of MU control was profoundly destabilized.

Under HDBR conditions [50], changes in MU activity developed considerably slower revealing a distinctive two-phase character. In the course of the first phase (the first 30 days of HDBR), the duration of IPP and their variability increased similarly to DI. The slope angle between the abscissa of the regression curve describing the relationship between the IPP values and the standard deviation increased threefold, thereby indicating destabilization of the motoneuronal pool activity as in DI. The slope angle increase, especially clearly seen at an interval of 60 to 120 days of HDBR (phase 2), was linked to the appearance of exceptionally short (70–90 ms) and, vice versa, exceptionally long (250–350 ms) intervals. Note that the so-called duplets, pairs of spikes with 4- to 20-ms IPP were recorded in many cases. This type of activity was characteristic of MU with a frequency of not lower than eight pulses per second. On the whole, the modifications of the MU characteristics in the first phase of HDBR were similar to those observed in DI, apparently reflecting changes in the MU involvement order and in destabilization of the motoneuronal pool activity, which seem to be associated with a decrease in the activity of support afferent input. This suggestion is also favored by the increased tendency for various MUs to synchronize their activity observed in this period in both DI and HDBR.

In the second phase, beginning with Day 30 of HDBR, the IPP variability, as well as the tendency for MU activity to be synchronized, decreased; however, the increase of destructive processes in muscles and neuromuscular synapses again changed the characteristics of MU activity determining the appearance of extra-long and extremely irregular IPP.

Spinal Reflex Mechanisms

The studies of the characteristics of spinal reflex mechanisms in DI and HDBR confirmed the suggestion that there exists a relationship between spinal hypersensitivity and muscle and support unloading noted in postflight investigations [2, 51]. Under the conditions of both exposures, in the first 24 h the thresholds of the tendon and H-reflexes of upper and lower leg extensor muscles decreased, and the amplitude increased.

The dynamics of the development of changes in DI and HDBR was different. In DI, they developed quickly but were transient, smoothing away at three or four days of exposure. On the contrary, in HDBR, they developed slowly and were relatively persistent being retained for a long time. Note that with insignificant changes in the thresholds of reflex responses, the amplitude changes were substantial. For example, in 120-day HDBR, the tendon reflex amplitude in the first 14 days increased more than 4-fold. The changes in the H-reflex system were substantially less. Later, the amplitudes of both responses showed the tendency to decrease approximating to the control values at 60–90 days of HDBR.

A similar directionality of the amplitude of the changes of the amplitude noted in the H-reflex indicated a significant contribution of the processes developing in muscle fibers in hypokinesia during development of these changes.

The Mechanisms of Motor Disorders in Weightlessness

Summing up the results of ground-based simulations studies, we cannot help pointing out that the experimental analysis of the phenomena noted under actual weightlessness conditions allowed us not only to describe them quantitatively but also, what is more important, to reveal their nature and the cause-and-effect relationships. Based on the data of these investigations, the notion of the leading role of support afferentation in the control of postural-tonic activity and its trigger role in the development of the motor effects of weightlessness was formulated.

The goal of subsequent systematic investigations also performed using ground-based simulation experiments, predominantly immersion, was to test and to develop this hypothesis [52]. When formulating the tasks of these studies, we thought it important to look into the role of support afferentation in the regulation of structural and functional characteristics of the tonic muscle system under the conditions that maximally exclude the influence of other concomitant factors of weightlessness—functional vestibular apparatus disorders, changes in the biomechanics of movements—and offer the possibilities of the quantitative assessment of the contribution of support stimulus to determining one or another characteristic of the muscle system.

The studies were performed under the standard DI conditions. The duration of immersion exposures was 7 h (the first series) and 7 days (the second series). In each series, the test pilots were subdivided into two equal groups conventionally designated as immersion (IMM) and immersion + support (IMM + SUP) ones. In the first group, the subjects were exposed to DI throughout the experimental period. In the second group, in the course of dry immersion, they were exposed to 20-min stimulation of foot support zones every hour for 6 h daily in the mode of slow (75 steps per minute) and brisk (120 steps per minute) walking.

Stimulation was performed using a SUC (support unloading compensator, a joint development of the IMBP and OOO Zvezda) device providing for alternate (walking rhythm) 0.4 kg/cm pressure on the foot supporting zones, calcaneous and tarsal ones.

The following lower leg muscle parameters were analyzed in the study: transverse stiffness measured with the autoresonance vibrography method (developed at the Institute of Applied Physics, Russian Academy of Sciences); the strength–velocity characteristics of isokinetic voluntary contractions; kinematic and electromyographic parameters of posture, locomotor and precision target movements; a number of structural and functional characteristics of muscle fibers important for understanding the mechanisms of the development of muscle contractile disorders under hypogravity: the size of fibers, their myosin phenotype, the maximum isometric strength of its fibers, and its dependence on Ca^{2+} concentration.

The 7-hour and 7-day stay under DI conditions was accompanied in the IMM group subjects by a significant decrease in the stiffness of lower leg extensor muscles developing in the first hours of exposure to immersion [51–53]. In 7-day DI, at the end of the first 24 h of exposure, the stiffness of the main tonic muscle, m. soleus, lowered by an average of 30%. Simultaneously, a 40% EMG amplitude decrease was recorded at rest; on completion of DI, a significant (up to 20%) maximum isokinetic strength decrease, especially marked in the strength modes of contractions. The changes recorded at the same time intervals for lower leg flexors (m. tibialis) were reversed: the stiffness and the resting EMG amplitude values, initially significantly higher than those of m. soleus, considerably increased in DI: the former, by 25%; the latter, twice [51].

In the subjects who were subjected to mechanical stimulation of foot support zones during immersion, the above-described alterations of lower leg muscle functions were not revealed at all or were substantially less marked: the stiffness decrease of m. soleus in this group attained the significance values only at six days of exposure to immersion, and its resting EMG amplitude in the course of DI and the maximum isokinetic strength of the three-headed lower leg muscle after completion of DI were not observed at all. The stiffness and the electromyographic flexor (m. tibialis) activity values did not change in the stimulation group either.

The studies of the electromyographic pattern of locomotion—walking at a rate of 90 steps per minute—revealed in the IMM subjects a considerably lesser contribution of m. soleus, a tonic of the three-headed lower leg muscle, to realization of locomotions after DI: the EMG amplitude to area ratio of m. soleus and m. gastrocnemius (fast muscle head) equal to 0.8 before DI decreased to 0.5 after DI. Simultaneously, the EMG amplitude of the m. tibialis flexors was sharply (by 30–50%) increased, reflecting the immersion-evoked postural flexor attitude [51]. In the IMM + SUP group, modifications of the electromyographic pattern of locomotions after completion of immersion were reversed: the ratio of the m. soleus to m. gastrocnemius EMG amplitudes in walking revealed the distinctively predominant recruitment of m. soleus in its realization [54].

Similar results were obtained from cellular studies. After immersion, all IMM subjects showed a decrease in the maximum isometric strength of m. soleus fibers in the 28–57% range. In the IMM + SUP group, significant changes in maximum isometric strength were not revealed [51]. The same also held for the curve reflecting the dependence of the relative isometric strength of fibers on the negative logarithm of Ca^{2+} ion concentration [52]. In the IMM subjects, after staying under DI conditions, the curve shifted to the right giving evidence of decreased myofibril sensitivity to Ca^{2+} ions. In the IMM + SUP subjects, no significant changes were found in the curve [49, 55, 56].

The slow-twitch (type I) muscle fiber size decrease in the IMM subjects after 7 days of DI constituted 24.8%. Note that changes in the fast-twitch (type II) muscle fibers were less marked. After DI combined with support stimulation (in the IMM + SUP group), no significant changes in the fiber cross section area of m. soleus samples were revealed. After DI, m. soleus in the IMM group exhibited a significant (although quantitatively small—6%) reduction in the share of fibers containing slow isoforms of heavy myosin chains. In the IMM + SUP group, individual changes in the myosin phenotype after DI combined with support stimulation were differently directed and did not reveal any sustained tendencies [56].

Thus, support removal determined the development of marked changes in all the structures and mechanisms of the tonic muscle system that were liable to analysis and eliminated using support irritations in the course of immersion exposure.

Along with, and in a certain sequence after, the decrease in the activity of lower leg extensor muscles, other characteristic effects of a support-free environment were manifest: increased venous compliance and, hence, decreased orthostatic tolerance; reduction in the maximum strength of lower leg extensor muscles, changes in the activity of the spinal reflex and supraspinal motion control mechanisms that showed up in postural difficulties, improper locomotions, deterioration of the precision characteristics of voluntary movements; and in modulations of their coordination pattern.

The temporal dynamics of the disorders was different; however, the sequence of their manifestations remained unchanged in all the cases. The signs of increased lower leg vein compliance, not exhibiting dependence on muscle stiffness and strongly correlating with it in DI, were the first to appear with a latent time to 3–6 h [51]. Later, after 4–5 days of gravitational exposure, the maximum strength of lower leg extensor muscles markedly decreased. According to the data of M. R. Recktenwald, J. A. Hodgson, et al., the process of reorganization of the coordination system of "target" leg movements associated with an increase in the contribution of the fast head of the three-headed lower leg muscle (m. gastrocnemius) to the realization of movements and with a decrease in the contribution of the slow head (m. soleus) in monkeys was completed at 14 days of the SF [14, 57]. The changes in the properties of muscle fibers were still more gradual and progressive [55].

The dynamics of recovery of disordered functions after hypogravitational exposure repeated, in large measure, the pattern in the course of exposure revealing more labile (electromyographic activity, tone) and more torpid (muscle strength, muscle cell changes) components of the abnormality complex. For example, the orthostatic stability parameters recovered following DI over several hours, whereas the coordination pattern of voluntary and locomotor movements after a 10-day flight remained variable until postflight Day 11 [58]. Of special interest is the fact of virtually complete elimination of all the effects of a support-free environment in use of support stimulation under support unloading conditions described in this work.

As mentioned above, all the subjects from the IMM group showed a significant decrease in the maximum isometric strength of m. soleus fibers after DI. The changes revealed in this study were much more profound than in relatively short-term hypokinesia, being comparable with only the effects of SF and long-term hypokinesia. In the IMM + SUP group, we did not observe any significant changes in maximum isometric contraction. The application of support stimulation under the support-free environment conditions significantly prevented the strength decrease in individual m. soleus fibers.

The results of these investigations showed that support stimulation also prevented a decrease in myofibril sensitivity to free calcium ions. Under DI conditions, we observed a shift in the Ca^{2+}–strength curve to the right. No such curve shift was observed in the IMM + SUP group.

The cross section area of slow-twitch (type I) muscle fibers decreased by 24.8% under DI conditions. The changes in the fast-twitch muscle fiber size were less marked.

Support stimulation associated with DI prevented the development of its influences on the size of muscle fibers. In the samples of obtained m. soleus after DI combined with support stimulation, significant changes in the cross section area of the fibers were not revealed.

After seven days in DI, a significant reduction in the share of fibers containing slow-twitch isoforms of heavy myosin chains was detected for the first time in human m. soleus. This effect was not revealed after immersion combined with support stimulation.

Thus, a number of the parameters liable to changes under hypogravity conditions and influencing the functional possibilities of m. soleus fibers exhibited an obvious dependence on the state of support input. Proceeding from the assumption as to the support-dependent regulation of the background contractile activity of tonic muscles (tone), the maintenance of such an activity under support stimulation could explain the preservation of the structural and functional characteristics of muscle fibers.

On the whole, the data presented in the aggregate with the results of the earlier investigations, in particular, the results of analysis of changes in the activity of the motor units of the three-headed muscles of the lower leg under support-free conditions [16], allowed us to conclude that deactivation of the postural tonic system of the extensor muscles appears to be the primary response to the elimination of support load [50]. Other phenomena discovered under these conditions, e.g., facilitation of the flexor mechanisms showing up in the increase of the electromyographic activity of flexor muscles at rest and in a vertical stance, as well as an increased EMG amplitude of m. tibialis responses to the support stimulation; impairment of the contractile properties of lower leg extensor muscles and alterations of the activity of all the mechanisms regulating these properties; coordination rearrangements affording redistribution of the order of recruitment of muscles—more tonic or more phasic—in the performance of one or another motor task [58], are derivative, secondary phenomena realized via the mechanisms of central coupling (flexor facilitation), learning (coordination rearrangements), and electromechanical inactivation of muscle fibers modulating, in turn, the processes of intracellular signaling (cellular changes) [59].

Central Mechanisms of the Hypogravitational Motor Syndrome

The 21st century was marked by rapid development of cellular and molecular studies in the field of gravitational physiology of movements. Note that the attention of researchers was focused on the structural and functional transformations determined by gravitational unloading in the central regulation systems, which were hardly studied earlier. An important role in the development of this line of research in Russia was played by the teams of Kazan scientific institutions cooperating with the IBMP: the Kazan Institute of Biochemistry and Biophysics, Kazan Research Center, Russian Academy of Sciences, and the Kazan State Medical University.

Extensive research into the effects of gravitational unloading in the links of the system of spinal control of the structure and function of the muscle apparatus showed that gravitational unloading determined the development of profound changes in the activity of all links of the system. In particular, it was shown that at 35 days of antiorthostatic hanging, the transverse size of rats lumbar spinal cord enlargement was substantially decreased [60]. Simultaneously, the total protein content (up to 21%) in this spinal region decreased. Note that the size of cervical enlargement and the protein content in the extract of the cervical division of test and control animals did not differ.

In the other series of immunohistochemical investigations of the lumbar spinal cord, almost a twofold increase in the Hsp25 content was revealed in rat lumbar spine after 35 days of orthostatic hanging [61]. The intense precipitate of immunohistochemical reaction with antibodies against Hsp25 was localized in perikarya, especially in nerve cell processes. The increase in Hsp70 expression in the spinal cord of test animals was less marked than that of Hsp25 expression. No differences in immunohistochemical reaction were revealed after 35 days, but, according to the immunoblot analysis data, the Hsp70 level in test rats after hanging was also by 42% higher than in the control animals. The results obtained gave evidence of the fact that the development of the hypogravitational muscle syndrome entails the development of the compensatory–adaptive mechanisms in motoneurons (increased expression of Hsp25 and Hsp70) suppressing apoptosis in motoneurons. The studies of the dynamics of the changes in the cross section area of lumbar spinal cord and in the above-mentioned substrates in test animals at different hanging times showed that a significant reduction in the cross section area of the lumbar spinal cord was recorded as early as a week after the experiment onset. With further hanging (for 14 and 35 days), the area values did not change and did not differ from those at seven days of exposure.

Immunohistochemical studies of the lumbar spinal motoneurons in hanging rats revealed a drastic decrease in their capacity for the synthesis of one of the key enzymes—acetylcholine transferase (AT) controlling spontaneous quantum secretion of the motor receptor mediator. A decrease in choline acetyl transferase (CAT) expression in the spinal motoneurons is known to occur in neurodegenerative diseases whose pathognomonic sign is progressive muscle weakness [60]. After 35 days of hanging, the immunoblotting method revealed a 54% CAT level decrease in the spinal cord protein extract of test rats compared with the control ones. Taking into account that the activity of acetylcholine (AC) secretion mediated by electrical impulses has the lead in realization of neurotrophic control ones, the authors suggested that decreased CAT expression may affect AC synthesis and, as a consequence, result in a relaxation of neurotrophic control over the neuromuscular system. Note that the myoneural synapse is known to be the most vulnerable link in this respect.

Scientists at the E.E. Nikolsky lab in Kazan investigated the influence of support unloading on spontaneous quantum secretion of mediator in the synapses of muscles of different functional profiles. The loss of support by the animals induced alterations of the intensity of spontaneous quantum mediator secretion in lower leg synapses.

The phenomena recorded in the experiments with the suspension also revealed the following in the processes of neurotransmission under gravitational unloading: (a) a decrease of the level of acetylcholine mediator synthesis in the motor nerve endings of lower leg muscles (within 30%); (b) a sharp decrease of the efficiency of the mechanisms carrying out presynaptic autoregulation of the process of transmission of excitation from nerve to muscle; and (c) a change of the sensitivity of acetylcholine esterase to methyl uracil derivatives.

According to the authors' opinion, decreased intensity of mediator synthesis in the motor nerve endings may be the result of the earlier noted changes in the processes of synthesis of the enzyme acetylcholine transferase in spinal motoneurons. This conclusion was confirmed by the studies of the retrograde axon transport velocity that showed a substantial (more than twofold) decrease of transport velocity in the axons of spinal motoneurons innervating rat lower leg muscles after six days of support unloading. On the whole, the studies of neurotransmission revealed alterations linked to both the state of the mechanisms of exocytosis carrying out release of the mediator quanta and the state of presynaptic control of the neuromediator process.

These changes seem to determine the effect of reduction in the level of the muscle fiber membrane potential influenced by gravitational unloading that was revealed in our investigations and the studies of E.E. Nikolsky [62]. It should be noted that this phenomenon was first described by L. G. Magazanik in the 1970s in rats flown on the Progress SF. It may be suggested that the membrane potential changes determine, in turn, a 30% decrease in the velocity of the spread of contraction in human lower leg slow muscle fibers after 3–7-day DI and 7-day SF noted by Prof. A.A. Gidikov and research workers from the IBMP [10]. This decrease developed very quickly, being essential as early as at three days of DI, and, as a membrane potential decrease, was retained at this level for the period of exposure.

Considering the results of cellular and molecular investigations of the spinal mechanisms of motion control led us to the conclusion that the leading role in the pathogenesis of the gravitational motor syndrome is played by disorders in the activity of the central neuromechanisms including reduction of the level of acetylcholine mediator synthesis in motor nerve endings; an impairment of the process of mediator quantum secretion; a sharp decrease in the efficiency of the mechanisms carrying out presynaptic autoregulation of the process of excitation transfer from nerve to muscle; a considerable (2.5-fold) decrease in the velocity of retrograde transport in the axons of spinal motoneurons innervating lower leg muscles; and, accordingly, significant changes in the state of their spinal motor center. The structural and functional changes in tonic muscles induced by support deprivation were not linked to the development of destructive processes in motoneurons where alterations on long-term exposures in the support-free environment were of functional and reversible nature.

In this review, we considered the theoretical problems of gravitational physiology of the motor system without addressing the practical aspects, which, as a rule, were the final target of our studies. Along with this, the theoretical knowledge allowed us to optimize the system of warning and correction of disorders, which are a natural consequence of physical and support unloading in SF. The results of investigations allowed us to optimize physical training regimens and the methods of control of physical work capacity of cosmonauts in SF; the range of passive means of prophylaxis has been substantially expanded [4].

It should be noted that the development of hypogravitational atony and atrophy is not a process inherent only in weightlessness. Long-term hypodynamia and hypokinesia due to disease, aging, and specific working conditions, are also accompanied by the development of the above changes. Proceeding from these ideas, research workers from the Institute of Biomedical Problems, Russian Academy of Sciences, have been actively working for more than 20 years to introduce into neurorehabilitation practice the prophylactic means developed for weightlessness: the Adeli and Gravistat medical suits designed on the basis of the Penguin loading safe-wear spacesuit are widely used in rehabilitation of patients with infantile cerebral palsy. The same is true for Regent suit for adults that is successfully used in the practice of neurorehabilitation and reversal of the consequences of stroke and brain injuries [63, 64].

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