Report

The effects of long-term microgravity on autonomic regulation of blood circulation in crewmembers of the international space station

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Abstract

The article presents the results of space experiment "Pneumocard". The investigation involved all 25 Russian members of the ISS crew. The total of 226 sessions were made including 130 aboard the ISS, 50 prior to launch and 46 on return from mission.

The objective was to study effects of the spaceflight factors on autonomic regulation of blood circulation, respiration and cardiac contractility during long-duration mission. The purpose was to secure new research data that would clarify our present view of adaptation mechanisms.

Registered were the following signals: electrocardiogram, impedance cardiogram, seismic cardiogram, pneumotachogram, finger photoplethysmogram. A set of hard- and software was used.

Autonomic regulation of blood circulation by HRV analysis was investigated. It was shown that at the onset of a space mission parasympathetic involvement in regulation increases typically with subsequent mobilization of additional functional reserve. It guided the development of a functional states mathematical model incorporating the established types of autonomic regulation.

Our data evidence that the combination of HRV analysis, pre-nosology diagnosis and probabilistic estimate of the pathology risk can reinforce the medical care program in space missions.

Keywords

Cardiorespiratory system • Autonomic regulation • Adaptation mechanisms • Heart rate variability • Functional reserve • Strain degree • Stroke volume • Probabilistic assessment • Risk category

Imprint

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Introduction

One of the main targets of space microgravity is the cardiovascular system. The major underlying reason is liquids displacement toward the upper part of the body and consequent increase of relative blood volume in the pulmonary circulation and cerebral vessels. Concurrent reductions in energy expense and afferent signaling complicate blood circulation regulation and, consequently, sufficient blood supply to organs and tissues in this situation. Adaptive reactions of organism in space flight are much dependent on the functioning of the cardiovascular system and its controls. Studies of heart rate regulation performed by IBMP investigators with participation of cosmonauts onboard the orbital stations "Salyut" and "Mir" gave the initial insight into the paths autonomic regulation of blood circulation chooses to adapt to in long-duration space flight. Already then it was found out that shifts occur in autonomic balance and segmental and suprasegmental activities rearrange to secure successful functional adaptation of organism to microgravity [1, 2]. The recent advance in understanding autonomic regulation of the cardiovascular system in microgravity has been made owing to research experiments "Pulse" and "Pneumocard" onboard the International space station (ISS) [3]. Experiment "Pulse" (ISS missions 5 - 13) was focused on autonomic regulation of blood circulation and respiration during long stay in microgravity. Registered were ECG, pneumotachogram, and peripheral pulse with the help of a finger photoplethysmograpy sensor [4,5]. Experiment "Pneumocard" was started in ISS mission 14; sessions were performed by Russian crewmembers every month over 5 years (from March, 2007 till end of 2012) [6]. In this experiment, seismic cardiography and impedance cardiography were added. Concurrent synchronous recording of five parameters and implementation of a series of functional tests made it possible to assess autonomic regulation of circulation simultaneously with cardiac contractility and central hemodynamics, and to judge straight about adaptability of organism in different mission periods. In fact, "Pneumocard" was the first research in space that furnished abundant information about multiple cardiac parameters used in assessing the functional state of cosmonaut's organism and estimating the risk of pathology.

Experiment "Pneumocard" had the objective to acquire new data that would expand our knowledge of the mechanisms by which the cardiovascular system adapts to the conditions of long-duration space mission.

Matherials and methods

The following physiological signals were recorded in the experiment:

- Electrocardiogram (ECG);
- Impedance cardiogram (ICG) according to the classic Shramek technique using 8 disposable electrodes (four on the neck (one pair on the right and the other on the left side) and four electrodes on the thorax (one pair on the right and the other on the left side);
- Seismic cardiogram (SCG);
- Pneumotachogram (PTG);
- Finger plethysmogram (FPG).

Investigations onboard the ISS employed a set of hard- and software called "Pneumocard" (patent for "Compact mobile device for investigation of the cardiovascular system of cosmonauts aboard space vehicle" RF № 77783 dated 03 July, 2008). The Pneumocard set with electrodes and sensors was attached to the breast belt of cosmonaut and did not cause any discomfort during experimental sessions in microgravity. Logged signals were stored in board PC and downlinked via the Internet; besides, data files were copied to flashcards which returned to Earth with the crew.

Preparation for experimental session consisted of donning the breast belt; care was taken to position the SCG sensor (linear acceleration - voltage converter) in the area of heart projection. Pneumocard recorder was fastened to the belt also. The photoplethysmographic sensor (tissue optical density- voltage converter) was applied to the left long finger. The pneumotachographic sensor or a thermister (ambient temperature - resistance converter) was attached to nostrils. Figure 1 shows an ISS cosmonaut making preparations for the Pneumocard session.

Figure 1. An ISS cosmonaut making preparations for the Pneumocard session

Experimental session included recording at rest (5 minutes), functional testing at a fixed breathing rate (10 breaths per a minute over 3 minutes; 6 breaths per a minute over 3 minutes) and with maximal in- and expiration breath-hold. Standing test was performed additionally before launch and after landing.

Fragment of a record is illustrated in fig. 2. Below is an example of cardiac intervalogram recorded for heart rate variability analysis (HVR) in all the experimental sessions. The results were analyzed for determination of a large number of parameters, HRV parameters first and foremost as guides to the autonomic regulation of functions. This technique is broadly used in space medicine since the early piloted missions [7].

HRV analysis is an integral approach to the assessment of mechanisms regulating physiological functions in organism of human and animal; specifically it comprises investigation of total regulation activity, neurohumoral regulation of the heart, and sympathetic-parasympathetic ratio in the autonomic nervous regulation. Actual status of the sympathetic and parasympathetic activities is a result of a multicircuit and multilevel cardiovascular reaction; the blood circulation system keeps adjusting own parameters till it finally achieves the optimum heralding successful adaptation of the whole organism [8, 9, 10]. The method is based on identification and measurement of time intervals between ECG R-waves (R-R intervals), construction of cardiac interval dynamic series (cardiac intervalograms) and ensuing analysis of numeric series with the use of mathematical methods.

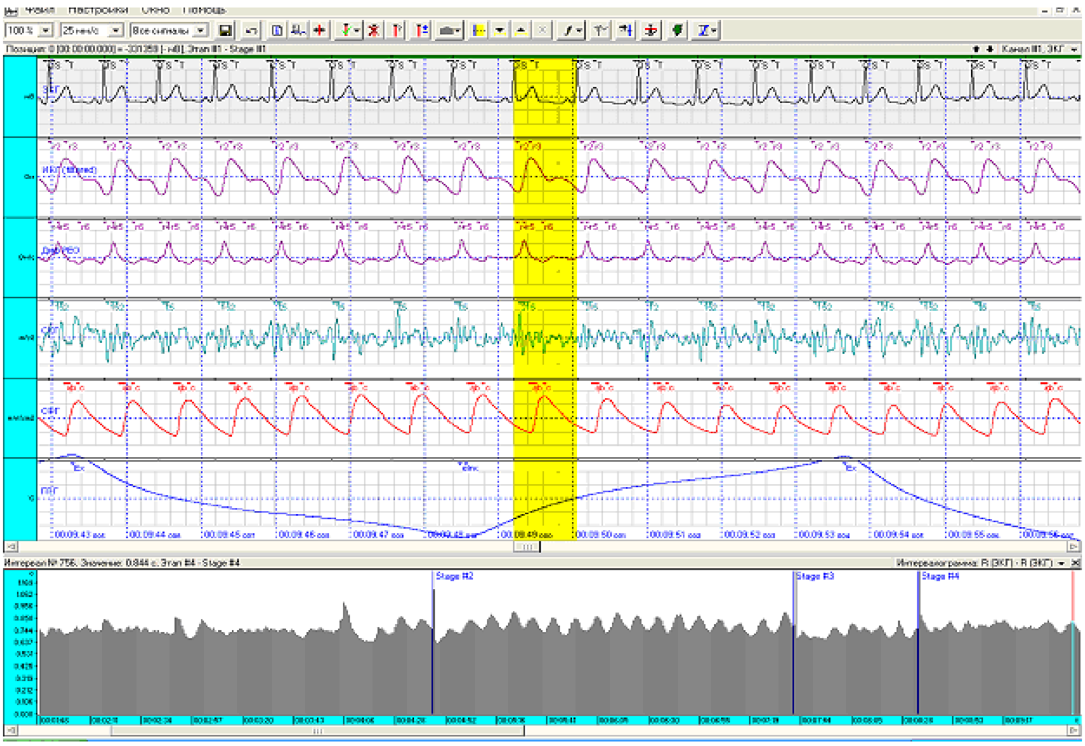


Figure 2. Example of a Pneumocard-recorded physiological signal. Top-down: ECG, impedance CG, first ICG derivative, seismic CG, finger photopletysmography, pneumotachography. Below – HRV at rest, at fixed breathing rate, and during in- and expiration breath-hold.

Advanced approaches were applied to analyze and assess information obtained in the space experiment. Space medicine has framed a fundamentally new concept of health evaluation with reference to the present-day postulates of the theory of adaptation and homeostasis teaching [11]. The concept asserts that health is a process of continuous adjustment of organism to ambient conditions; measure of health is organism adaptability. Degradation from health to disease is linked to reduction of the adaptive potential, loss of the ability to respond adequately to socio-occupational and everyday stresses. On the borderline between health and disease many transitory states known as pre-nosology may develop [12, 13]. Results of investigations are considered in terms of pre-nosology diagnosis concerned with the states in-between the norm and pathology. The staple method of pre-nosology diagnosis is heart rate variability analysis (HRV). It served as a cornerstone for mathematical modeling of the functional states of organism in which the states plane is specified by two main parameters: DT (degree of tension) and FR (functional reserve). The mathematical model inspired the development of the probabilistic approach to pathology risk estimation [14].

Results and Discussion

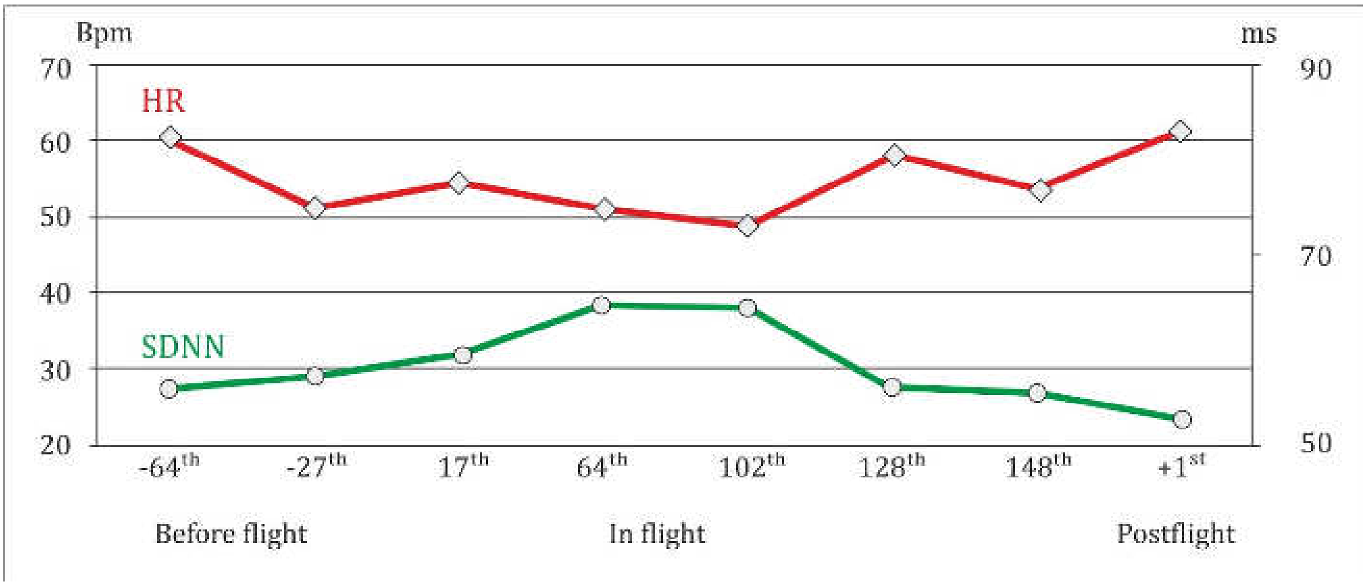
A. Cardiovascular system adaptation to microgravity

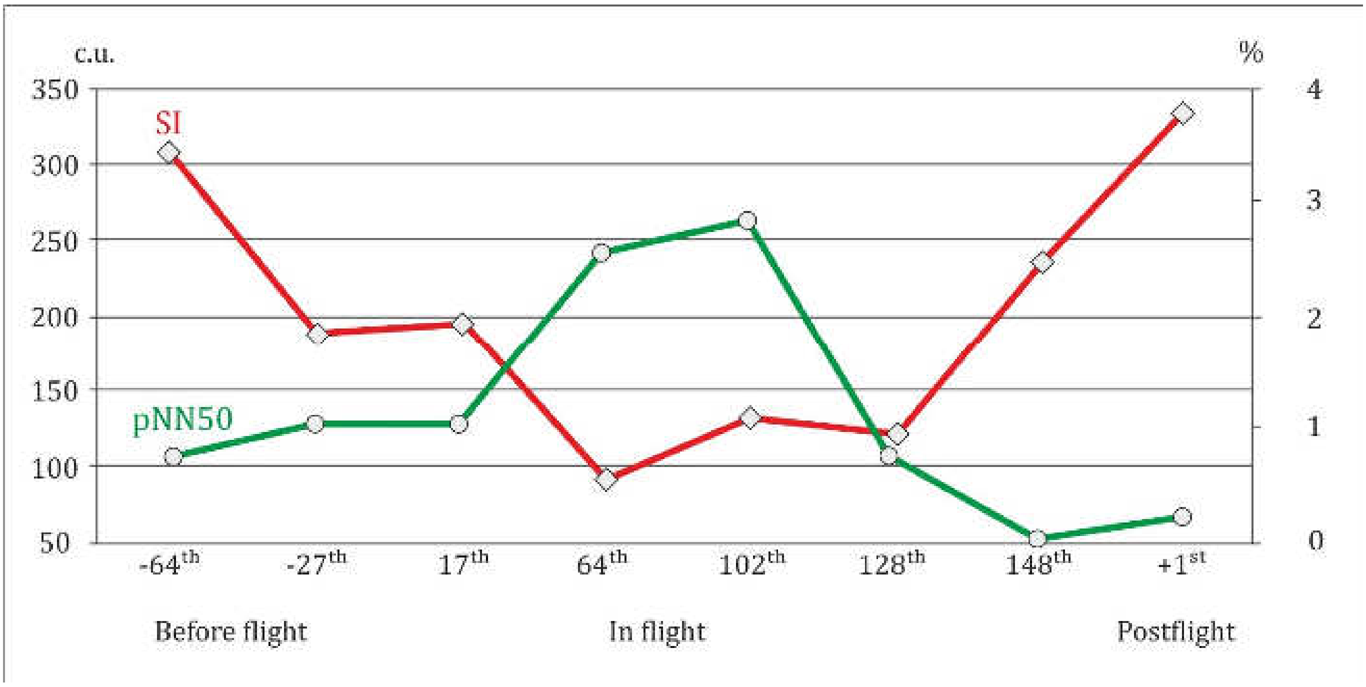
Role of autonomic regulation

Adaptation processes are aimed at setting equilibrium between organism and environment. The processes are stipulated by mechanisms of autonomic regulation; type of regulation is deduced from dynamics of the heart rate variability (HRV) parameters. Figure 3 (A, B, C, D) gives an example of specific autonomic regulation changes in a cosmonaut in different periods of a long-duration ISS mission. One can see that in orbit heart rate (HR) was 5-10 beats/min slower compared with the pre-launch measurement; HR on the landing day was equal to pre-launch. During the first half of the mission SDNN demonstrates a strong trend upward (from 26 ms to 39 ms) and then goes down till return to initial values at the end of mission. Yet, a more detail analysis of the in-flight autonomic balance reveals rather complex dynamics.

In the pre-flight investigation, the cosmonaut was characterized by a high sympathetic tone. Stress index values (SI) amounted to 189-306 conventional units remaining 184 conv. units on mission day 17. As figure 3B shows it, further in mission SI made a decrease against a distinct rise in pNN50. For instance, on MD-102 SI decreased to 135 conv. units which was necessitated massive mobilization of the functional reserve of regulation.

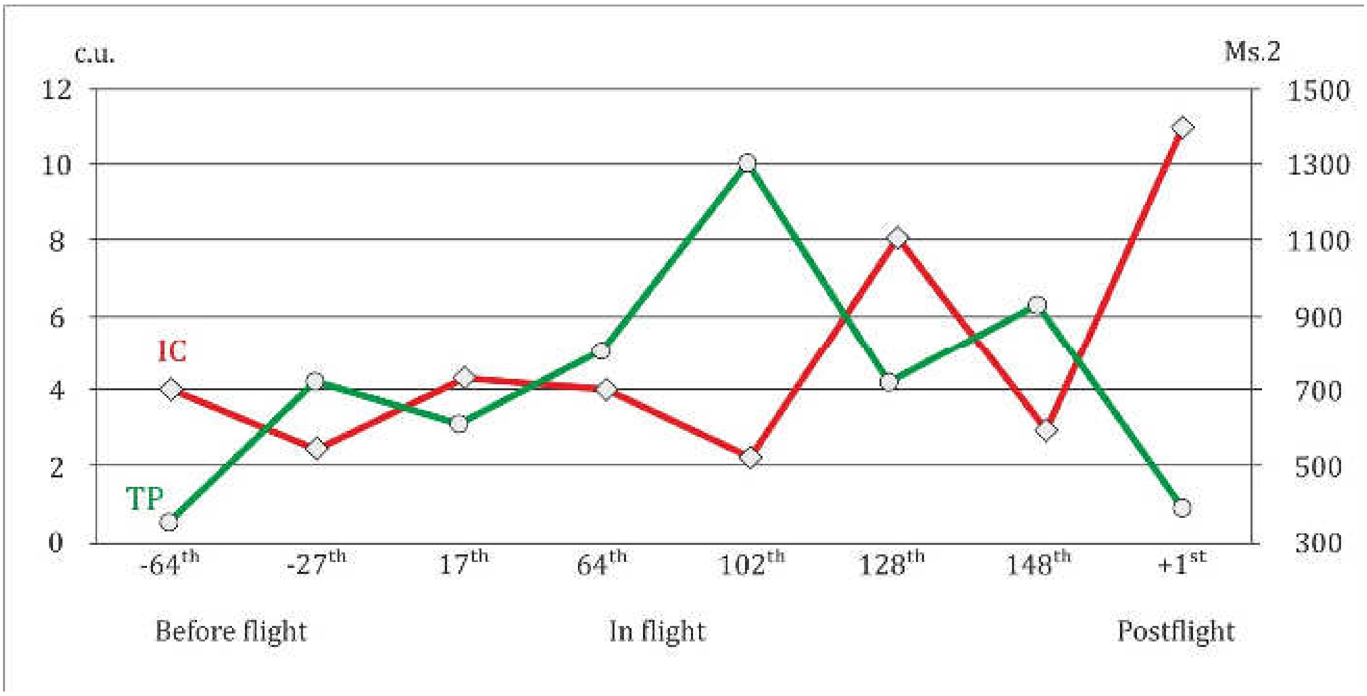
Figure 3C presents curves for TP (HRV total power) and IC (regulation centralization index) according to which the total spectral power tripled on MD-102 in comparison with pre-launch values. At the same time, centralization index (CI) almost halved.





Also, the maximum in absolute value calculated for HRV low-frequency power (LF) was the result of blood pressure regulation (fig. 3D).

On MD-128, regulation by the subcortical vascular center persisted as is apparent from still high absolute, and maximal LF relative values (fig. 3D) reaching 75 %. In its turn, CI rises to 7.8 in relative units due to the high LF value.



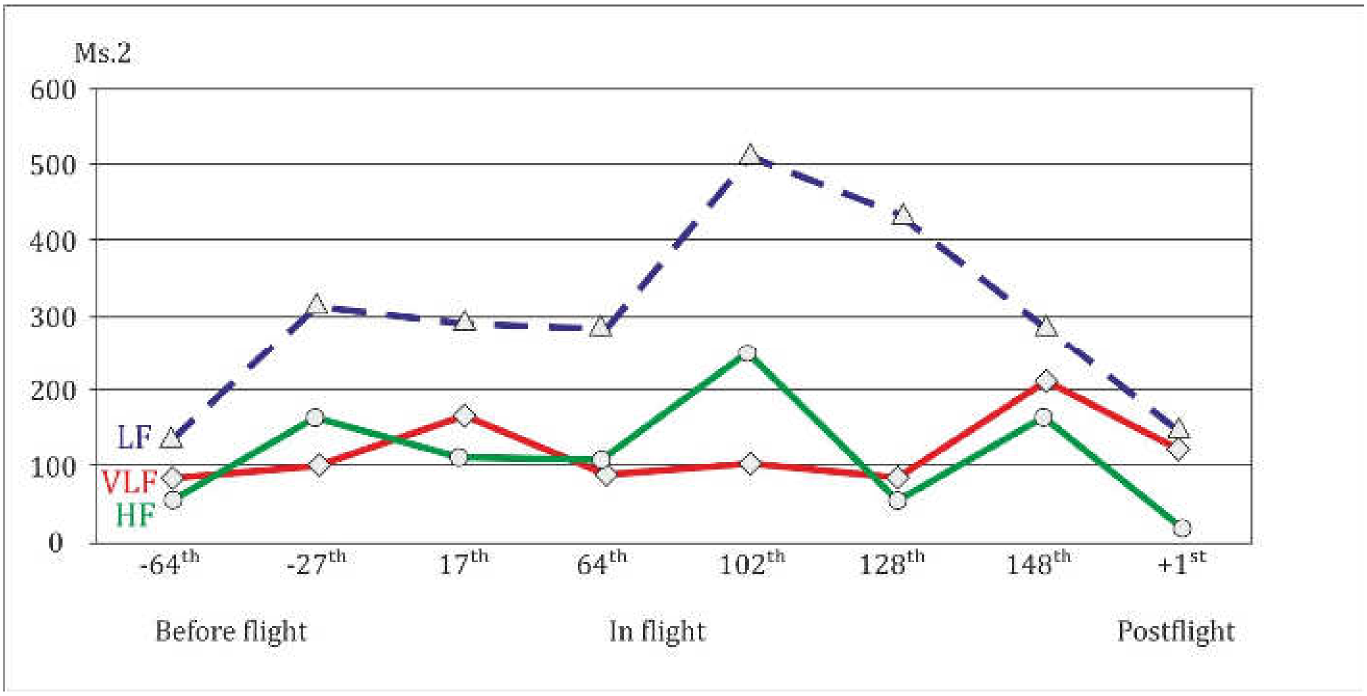


Figure 3. Changes in HRV parameters in a cosmonaut in the course of ISS mission. HR (heart rate) and SDNN; SI (stress index) and pNN50; TP (total spectral power) and IC (index of centralization); Involvement of specific parts of the autonomic regulation system (HF – parasympathetic regulation; LF - sympathetic regulation of the vascular tone; VLF - segmental and suprasegmental regulation of energy metabolism).

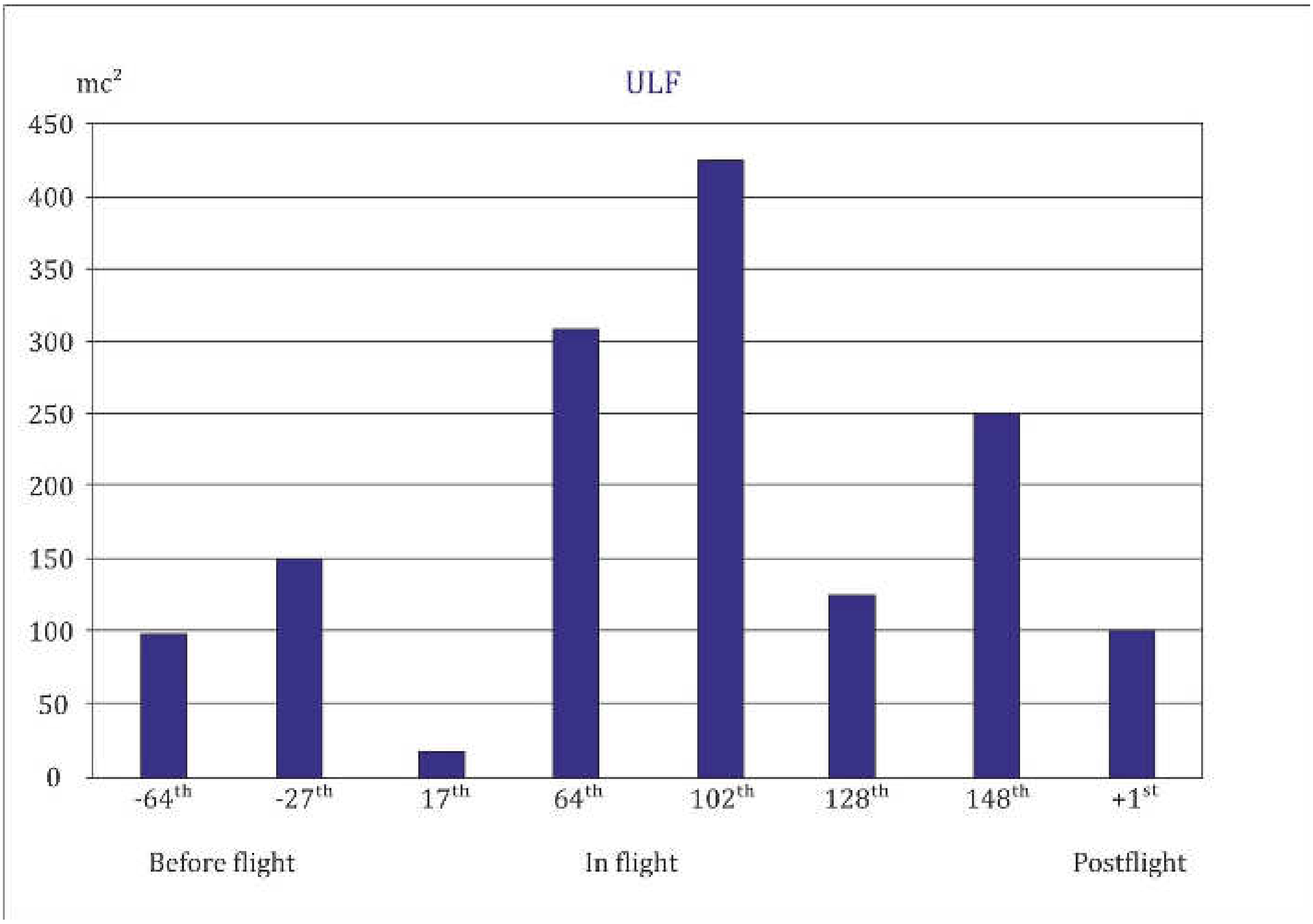


Figure 4. HRV ultralow-frequency power (ULF) dynamics in an ISS cosmonaut

Looking closely into the vascular tone regulation on MD 102 and 128 it can be noted that HR and SI had relatively normal values in the cosmonaut. In this context, we should turn our attention to dynamics of the ultralow-frequency HRV spectrum (ULF) presented in figure 4. On MD-102, the parameter was at its maximum (435 ms^2 versus 102 ms^2 before launch) which is attested by high activity of the suprasegmental centers in the brain. Consequently, there is good reason to tie up these changes in vascular regulation with hypothalamo-pituitary involvement, i.e. mobilization of the higher autonomic centers. These phenomena can be caused by fatigue, poor sleep or psycho-emotional strain.

By the end of mission (MD-148) stress-index is again on the rise (up to 238 conv.units) while pNN50 drops sharply (fig. 3B); very low frequency power (VLF) grows as high as 219 ms^2 in comparison with 78 ms^2 before launch. It means that sympathetic regulation becomes more influential because of the need to mobilize the functional reserve. Abrupt reduction of the functional reserve by the mission end reveals itself by the conspicuous stress reaction in the post-landing period. From figure 3 (B-C) it is evident that after landing stress index grew to 335 conv. units and that index of centralization reached 11.4.

The above character of autonomic regulation dynamics essentially depends on individual peculiarities of the regulation mechanism. Table 1 provides data on individual patterns of autonomic regulation in Russian members of ISS crews in different mission periods. Based on these data, there is no direct correlation between the results of pre-launch investigations and those obtained in and post flight. However, cosmonauts' reactions have similarity with the extreme types of autonomic regulation. For instance, К-10 and К-13 who exhibited the highest pre-launch heart rate and SI values both had high HR post flight (112 and 85, respectively); besides, К-10 had the highest SI (915). At the same time, although pre-launch HR in К-6 was the lowest (52), his post-landing PR also measured very high (84).

Values of HRV total spectral power (TP) that characterize level of the regulation functional reserve are in no way predictors. For instance, in К-16 TP values were the highest during mission (2200-6000) and relatively high before launch (3480), whereas in К-14 TP was the highest before launch (8000) but no metamorphosis was observed in autonomic regulation either during or after mission. These observations instigated the development of alternative methods of functional state assessment with account of type of autonomic regulation.

Table 1. Individuality of autonomic regulation in cosmonauts in different ISS missions periods (experiment "Pneumocard")

ISS cosmonauts	Heart rate variability parameters								
	Before launch			In mission			After mission		
	HR	SI	TP	HR	SI	TP	HR	SI	TP
1	71	177	2735	63-68	70-180	4800	76	544	2864
2	63	65	2270	58-82	44-103	1500-3100	97	680	430
3	67	165	835	48-57	34-108	1000-2500	67	86	690
4	66	98	1130	65	212	480	105	590	380
5	63	77	1550	64-77	30-130	1130-3100	80	258	470
6	52	23	3860	55-59	27-68	2000-6500	84	177	1200
7	70	101	1670	48-55	22-62	1750-3600	63	48	4370
8	59	64	2100	66-75	108-183	750-1450	71	156	920
9	56	66	2030	46-71	21-61	1960-5350	73	52	3070
10	85	400	360	68-78	100-270	500-1700	112	915	1900
11	58	100	1200	51-57	40-165	790-4000	57	68	1150
12	68	105	1300	64-71	45-89	2200-3100	82	84	2140
13	89	270	1000	66-80	48-70	2200-3100	85	100	1300
14	65	25	8000	62-70	25-154	1000-5000	57	50	2750
15	55	130	450	55-61	75-102	800-3600	61	142	1000
16	60	26	3480	45-60	22-50	2200-6000	83	280	530
17	75	190	720	73-80	90-240	600-1300	83	340	410
18	70	88	1700	53-65	30-53	970-5100	64	65	2050
19	68	90	2140	62-74	57-110	800-2100	81	360	420
20	67	124	1600	53-68	45-90	1650-4500	69	136	860
21	72	65	1980	62-69	70-140	620-2700	83	112	1870
22	71	47	1800	58-62	30-70	1800-3500	61	30	8000
23	58	114	1200	64-71	71-200	600-2500	78	181	1196
24	57	98	1500	45-52	40-63	985-2500	67	116	3555
25	67	77	1800	59-70	117-240	340-1160	69	280	760

B. Pathology risk estimation

Risk of pathology development in the course of mission was estimated using a mathematical model of the functional states of organism built on the generalized results of heart rate variability analysis in all Russian cosmonauts who had made long-term missions to the ISS [15].

The model represents a system of two discriminant function equations; one equation describes strain degree of regulation straining (SD) and the other, regulation functional reserve (FR). Magnitudes of SD and FR are calculated from HR, pNN50, SI and HF,%. Besides, consideration is given to individual type of autonomic regulation. SD and FR values are used to form a phase plane as a two-dimensional space of the functional states. Each of four quadrants in the space corresponds to one of four functional states: physiological norm, pre-nosology, premorbidity and pathology.

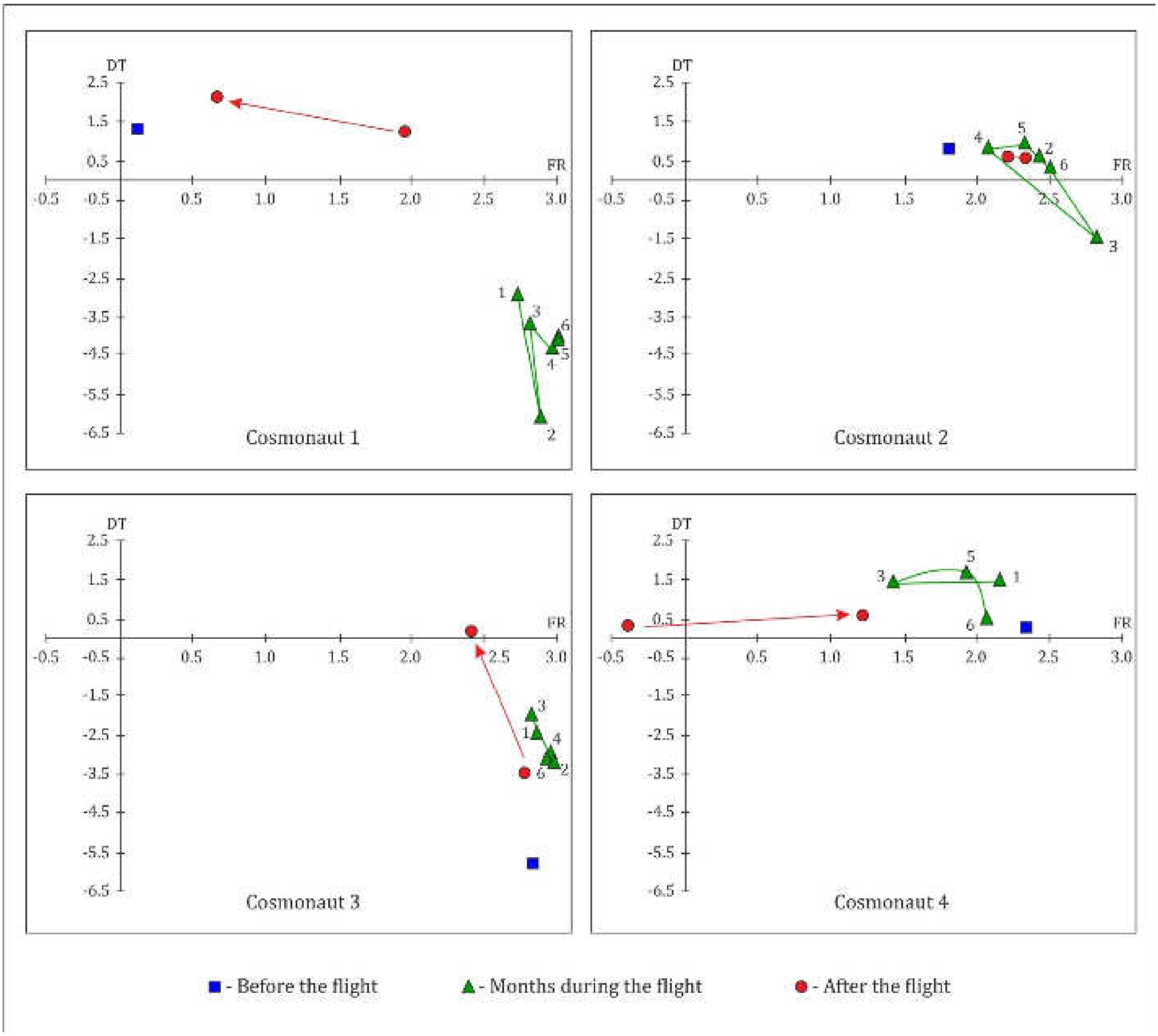


Figure 5. Functional state dynamics in four cosmonauts on space missions (phase plane trajectory). Abscissa – FR (functional reserve), ordinate – DT (degree of tension).

During every investigation the actual functional state is determined as a point with coordinates SD and FR; variations in the functional state in the course of mission are displayed as a phase plane trajectory. Figure 5 illustrates the functional state trajectory in four ISS cosmonaut during mission. As zone. By the mission end the pre- nosology character of functional state becomes even more evident reaching the pre-launch level and moves to the premobidity borderline after landing

Following every experimental session, functional states probability was calculated from DT and FR values with consideration of a person-specific type of autonomic regulation. Each point in the states space has continuation in the future and, therefore, can be estimated using methods of the mathematical probability theory. The actual functional state is the most probable one, and yet it is also possible to judge about probability of functional state evolution down to pathology.

To assess the risk of pathology, a risk classification system was set up by IBMP investigators [14]. The rating scale has reference to 10 risk categories. The first three categories lie within a relatively safe zone of the functional states, categories 4-5 suggest presence of debilitating factors, categories 6-7 call for urgent measures to be taken to optimize living and labour conditions; category 8 and above indicate the necessity of nondelayed risk mitigation. Figure 6 presents risk categories established for K-17 at different time points of the investigation. According to these data, his functional state was unfavorable prior to and after mission, and on mission day 148.

Table 2 tabulates the results of functional state assessment in all Russian cosmonauts who participated in the Pneumocard experiment aboard the ISS. From the table it follows that before launch pre-nosology(PN) was diagnosed in 9 out of 25 cosmonauts and premorbidity (PM) in one cosmonaut. There were 16 pre-nosology episodes during missions. On return from orbit, pre-nosology was observed in 13 cosmonauts; functional state of 5 cosmonauts was qualified as premorbid. From this follows the conclusion that the overall stress-effect of the spaceflight factors on human organism is rather detrimental, for pre-nosology was diagnosed 1.5 times more frequently on mission than earlier on the ground and 20% of cosmonauts exhibited premorbidity after return from the ISS. Mean risk categories were equal to 2.08, 3.04 and 3.36 before, in and after mission, respectively. Based on this evidence, combination of HRV analysis with the probabilistic approach and application of the methods of pathology risk estimation can be advantageously adopted by the system of spacecrew health monitoring.

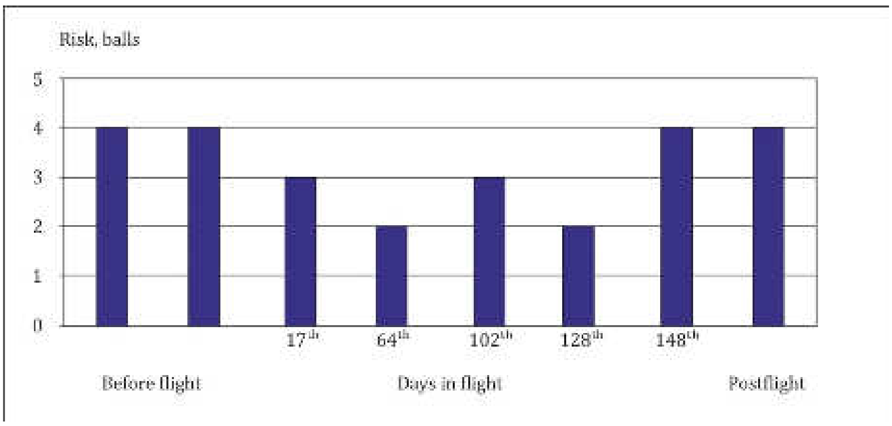


Figure 6. Risk categories established for K-17 at different time points of the investigation

Table 2. Functional state of the ISS cosmonauts according to the “Pneumocard” data

ISS cosmonauts	Before launch	During mission	After return	Risk category
1	Д	N	N	4-3-3
2	N	N-PN -N	PN	1-4-6
3	N	N	N-PM	3-3-7
4	N	N-PN	PM	1-6-9
5	N	PN-N	PN	1-4-3
6	N	PN-N	PN-N	1-5-3
7	N	N	N	3-2-1
8	N	N	N-PN	2-3-3
9	N	N	N	2-1-1
10	PN	PN	PM	4-4-8
11	PN	PN	PN	2-4-2
12	PN	N -PN	PN	3-3-4
13	PM	PN	PN	5-2-2
14	N	N –PN - N	N	1-4-1
15	PN	PN	PN	2-3-2
16	N	N	PN -N	1-2-4
17	PN	PN	PN	4-4-4
18	PN	PN - N	N	1-2-1
19	N – PN	N - PN	PM -PN	2-2-4
20	PN	PN	PN	2-3-2
21	N	PN N- PN	PN - PM	1-2-4
22	N	N	PN - N	1-1-3
23	N	N – PN	N	3-4-2
24	N	N	N	1-2-2
25	N	N – PN	PN –N	1-3-3

Conclusions

Space experiment “Pneumocard” made a milestone in the advance of space medicine, space cardiology specifically. First and foremost, this was not a one-off experiment but a great series of systematic purposeful investigations of the cardiorespiration system scheduled for every month and continued by the ISS cosmonauts over more than 5 years. We should emphasize the unprecedented nature of the experiment. Its findings gained acceptance at many Russian and international symposia and conferences [2, 3, 4, 5, 16, 17, 18, 19, 20, 21]. Their theoretical significance arises from demonstration of the role played by autonomic regulation in providing cardiovascular homeostasis in long-duration space mission. The experiment enabled elicitation of mechanisms through which autonomic balance rearranges in different periods of long exposure to microgravity, and setting the criteria of autonomic regulation assessment based on HRV analysis. Finally, the experiment evidenced that to a large degree adaptation of human organism to microgravity is dependent on individual type of autonomic regulation.

Applicative implications of the results of our investigation are determined by two outcomes: 1) successful testing of the technique for identification of individual type of autonomic regulation in spacecrew members; 2) development of the probabilistic approach to estimation of the risk of pathology in the conditions of long-duration space mission as an instrument for predicting functional state degradation in crewmembers. Both outcomes have the potential to gain footing as in space medicine, so in different fields of applied physiology delving into the adaptive reactions of human organism to extreme environments. Space medicine is committed to promotion of cutting-edge space technologies to healthcare and, at the same time, to integration of the latest achievements of medical sciences into the system of spacecrew medical care and life support.

Statement on ethical issues

Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest

None declared.

Author contributions

All authors prepared the manuscript and analyzed the data, A.G.C. drafted the manuscript. All authors read the ICMJE criteria for authorship and approved the final manuscript.

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