

## Vestibular Function after Repeated Space Flights

I. A. Naumov<sup>a,\*</sup>, L. N. Kornilova<sup>a</sup>, D. O. Glukhikh<sup>a</sup>, A. S. Pavlova<sup>a</sup>, E. V. Khabarova<sup>a</sup>,  
G. A. Ekimovsky<sup>a</sup>, and A. V. Vasin<sup>b</sup>

<sup>a</sup> Institute of Biomedical Problems, Russian Academy of Sciences, Moscow, Russia

<sup>b</sup> Gagarin Scientific Research Cosmonaut Training Center, Zvezdnyi, Moscow oblast, Russia

\*e-mail: naumovivan@gmail.com

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**Abstract**—This paper presents the results from testing the vestibular function on return from repeated space flights (SF) in 32 cosmonauts of the International Space Station that were in long SFs of 125–215 days. The cosmonauts were tested twice before the flight (baseline data collection) and on days 1–2, 4–5, and 8–9 after landing. The testing was made using two methods for recording eye movements (with simultaneous recording of head movements): electro-oculography and video-oculography. It is shown that the repeated stay in the long SF leads to a considerable statistically significant reduction in the de-adaptation period. Atypical vestibular disorders and changed patterns of the otolith-semicircular canal interaction are observed mostly in the cosmonauts who have made their maiden flights to microgravity.

**Keywords:** vestibular system, otolith-cervico-ocular reflex, vestibular-cervico-ocular reflex, vestibular reactivity, microgravity

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Analysis and processing of the results from studying the vestibular function in a joint (common) group of cosmonauts after long space flights (SFs) revealed a number of regular changes in the vestibular system [1–3]. However, the Questionnaire experiment [3] and cosmonaut surveys conducted after the SFs showed that in-flight adaptation and subsequent re-adaptation to terrestrial conditions proceeded much easier and faster in the case of repeated SFs. In this connection, it is necessary to obtain objective data that characterize the real state of the vestibular system of the cosmonauts.

### METHODS

The study was conducted in the course of the Sensory Adaptation pre-flight and post-flight experiment and Assessment of the Vestibular Function clinical

and physiological examination. Thirty-two Russian crewmembers of the ISS-8–ISS-32/33 missions who were in the SFs of 125–215 days were examined. The age of the cosmonauts ranged from 35 to 54 years.

The scientific and methodological note of the experiment was reviewed and approved by the Commission on Biomedical Ethics of the Institute of Biomedical Problems (IBMP RAS) and Human Research Multilateral Review Board (HRMRB), and the cosmonauts themselves signed an informed consent to participate in the scientific experiment.

During the processing of the data, the cosmonauts were grouped as follows: the general group, group 1 (the cosmonauts who were in the SF for the first time), group 2 (the cosmonauts who had a preliminary SF experience) (Table 1).

The cosmonauts were examined twice before the SF (60–30 days before the SF, the baseline) and on

**Table 1.** Groups of the examined cosmonauts

Groups of the cosmonauts	Number of people	Age range, years	Preliminary experience of stay in microgravity	Interval between the SFs, years	Duration of the SF, days
Common group	32	35–54 (~45)	0–624	2–8	125–215 (~175)
Group 1	18	35–53 (~43)	–	–	125–199 (~176)
Group 2	14	38–54 (~48)	129–624 (~342)	2–8 (~4)	125–215 (~175)

\* The mean values of the corresponding ranges are given in the brackets.

days 1–2, 4–5, and 8–9 after the SF, in a number of cases, on day 13–14 (according to the indications).

The experiment was carried out using a set of computer stimulation programs specially developed by the specialists of the IBMP RAS [1–4] that determines the following:

- Spontaneous eye movements (SEMs).
- Static torsion otolith-cervico-ocular reflex (OCOR).
- Dynamic vestibular-cervico-ocular reflex (VCOR) and vestibular reactivity (VR).

The study was performed using two methods for recording eye movements (with simultaneous recording of head movements): electro-oculography (EOG) and video-oculography (VOG).

#### *Spontaneous Eye Movements*

The following parameters were determined: roving and saccadic eye movements, eye tremor, spontaneous nystagmus and gaze evoked nystagmus at the central position of eyeballs and in the lateral turnings alternately to the right, left, up, and down with the eyes closed (EOG method) and eyes open (VOG method) at the corresponding sound command. The eyes were held in each position for 7 s with the execution of one test iteration.

The investigation of spontaneous eye movements was carried out with the immovable head fixed in the upright position with the use of a soft-fixing head holder (the so-called Shantz collar).

#### *Static Torsion Otolith-Cervico-Ocular Reflex*

The study of the OCOR consisted of estimating the amplitude of the compensatory eyeball counter-rotation at head inclinations and was performed by the VOG method during head inclinations at the sound command alternatively to the right and left shoulder at an angle of 30°. The value of the head inclination angle was recorded by sensors of the VOG helmet and was monitored by means of a special fleximeter. While performing the test, a cosmonaut alternatively made two head inclinations to each shoulder.

#### *Dynamic Vestibular-Cervico-Ocular Reflex and Vestibular Reactivity*

The VCOR was estimated based on the amplitude and speed of compensatory eyeball counter-rotation when rotating the head around the longitudinal body axis (in the horizontal plane) at a frequency of 0.125 Hz with closed eyes (the EOG method). The number of test iterations ranged from six to nine.

VR was estimated based on the nature, intensity, and quantitative indices of nystagmus that overlaps the compensatory eyeball counter-rotation reflex during the test for studying the VCOR.

#### *Recording of Eye and Head Movements*

Eye movements were recorded by the EOG method using the OkuloStim hardware and software system (joint development of the specialists from the IBMP RAS and Statokin Scientific Medical Company) [1–3] that includes an oculotahoniograph, a direct-current four-channel amplifier with a sampling frequency of 250 Hz for recording eye movements and an external three-axis accelerometer combined with an angular speed sensor with a sampling frequency of 100 Hz for recording head movements. The final accuracy of recording and processing EOG data was  $\sim 0.5\text{--}1^\circ$ .

Horizontal, vertical, and torsional eye movements were recorded by the VOG method using a Chronos Vision ETD system (Chronos Vision, Germany) [5, 6]. The cosmonaut's head was covered with a helmet equipped with infrared cameras with a frequency of 200–400 Hz for recording eye movements (an accuracy of  $<0.05^\circ$  for all three components) and three-axis accelerometer and angular speed sensor for recording head movements.

The following parameters were estimated when processing the eye-movement reflexes:

—The amplitude of compensatory torsion eyeball counter-rotation in the static head position after inclining to the shoulder (the amplitude of the OCOR) and gain factor of the OCOR (gfOCOR) that is the ratio of the angle of compensatory torsion eyeball counter-rotation to the head inclination angle.

—The gain factor of the VCOR (gfVCOR), which is the ratio of instantaneous angular eyeball counter-rotation speed to the instantaneous angular head movement speed that is averaged over the head rotation period.

—The time, amplitude, speed, and frequency characteristics of nystagmic reflexes (including the amplitude of the rapid nystagmic phase  $A_{Ny}$ , speed of the slow nystagmic phase  $V_{Ny}$ , nystagmic frequency  $F_{Ny}$ , relative duration of the nystagmus  $T_{Ny}$ , which is the ratio of the total duration of nystagmic cycles to the total duration of the test).

The statistical analysis of the results of the study was carried out using the tools of the MathWorks Matlab mathematical software package. In all cases of checking the statistical hypotheses (normality of distributions, homogeneity (equality) of variances, reliability of differences, etc.), the level of significance  $\alpha$  was 0.05. The hypotheses about the presence of statistically significant changes in the parameters before and after the flight were tested using both parametric and non-parametric methods of variance analysis:

—The  $F$  test (ANOVA) for repeated measurements with multiple sample comparisons by the Tukey–Kramer and Newman–Keuls tests.

**Table 2.** Spontaneous eye movements before and after the SF

Groups of the cosmonauts	Before the SF	Day 1 after the SF	Days 4–5 after the SF	Days 8–9 after the SF
Group 1 (18 subjects)	Normal in all cosmonauts, except one	Normal—22% Elevated—33% Nystagmus—45%	Normal—50% Elevated—8% Nystagmus—22%	Normal—67% Elevated—3%
Group 2 (14 subjects)	Normal in all cosmonauts	Normal—58% Elevated—1% Nystagmus—21%	Normal—79% Elevated—21%	Normal in all cosmonauts

—The Friedman ANOVA test with pairwise sample comparisons by the Wilcoxon and Mann–Whitney tests with the Bonferroni correction.

The normality of distributions was verified by the Lilliefors test, the homogeneity of variances was checked by the Levene test, and the presence (absence) of pair correlations between the investigated parameters was checked using the Pearson and Spearman correlation coefficients.

**RESULTS AND DISCUSSION**

Analysis of the common group of the cosmonauts revealed statistically significant differences between the pre-flight and post-flight data [1–3]. However, due to the high sample variability, groups 1 and 2 were analyzed separately, which revealed statistically significant differences between the groups (the Mann–Whitney test).

*Spontaneous Eye Movements*

Before the SF, all cosmonauts, with the exception of one, had a stable oculogram. One cosmonaut from group 1 was recorded to have gaze evoked nystagmus in both horizontal and vertical turning of eyes when looking at the center ( $A_{Ny} = 2.5 \pm 0.3^\circ$ ,  $V_{Ny} = 4.3 \pm 0.8^\circ/s$ ,  $F_{Ny} = 0.5 \pm 0.04$  Hz).

The estimate of SEM before and after the SF is presented in Table 2.

In group 1 on day 1–2 after the flight, SEM was normal in 22% of the cosmonauts; 33% had an intensified SEM in the form of roving eye movements (the so-called slow wave drifts) and saccadic eye movements that predominately had a rectangular shape (the so-called square wave jerks); the remaining 45% had a spontaneous nystagmus ( $A_{Ny} = 3.8 \pm 0.6^\circ$ ,  $V_{Ny} = 6.5 \pm 0.8^\circ/s$ ,  $F_{Ny} = 1.5 \pm 0.1$  Hz,  $T_{Ny} = 18.6 \pm 7.1\%$ ) and gaze evoked nystagmus ( $A_{Ny} = 3.1 \pm 0.7^\circ$ ,  $V_{Ny} = 3.7 \pm 0.8^\circ/s$ ,  $F_{Ny} = 0.6 \pm 0.1$  Hz,  $T_{Ny} = 34.9 \pm 12.5\%$ ).

On days 4–5 after the flight, SEM was normal in 50% of the cosmonauts from group 1, 28% had an intensified SEM, and the remaining 22% had gaze evoked nystagmus ( $A_{Ny} = 2.8 \pm 0.7^\circ$ ,  $V_{Ny} = 3.4 \pm 0.6^\circ/s$ ,  $F_{Ny} = 0.4 \pm 0.09$  Hz,  $T_{Ny} = 16.1 \pm 7.7\%$ ).

On days 8–9 after the flight, SEM was normal in 67% of the cosmonauts from group 1, and the remaining 33% had an intensified SEM of the saccadic and roving nature with a full recovery of SEM on days 13–14.

In group 2 on days 1–2 after the flight, SEM was normal in 58% of the cosmonauts, 21% had an intensified SEM, and the remaining 21% had spontaneous nystagmus ( $A_{Ny} = 4.1 \pm 0.9^\circ$ ;  $V_{Ny} = 6.2 \pm 1.0^\circ/s$ ;  $F_{Ny} = 1.3 \pm 0.1$  Hz;  $T_{Ny} = 12.3 \pm 8.6\%$ ) and gaze evoked nystagmus ( $A_{Ny} = 3.3 \pm 0.8^\circ$ ,  $V_{Ny} = 3.8 \pm 0.9^\circ/s$ ,  $F_{Ny} = 0.7 \pm 0.1$  Hz,  $T_{Ny} = 22.4 \pm 9.0\%$ ).

On days 4–5 after the flight, SEM was normal in 79% of the cosmonauts from group 2, and the remaining 21% had an intensified SEM. On days 8–9 after the flight, SEM was normal in all cosmonauts from group 2.

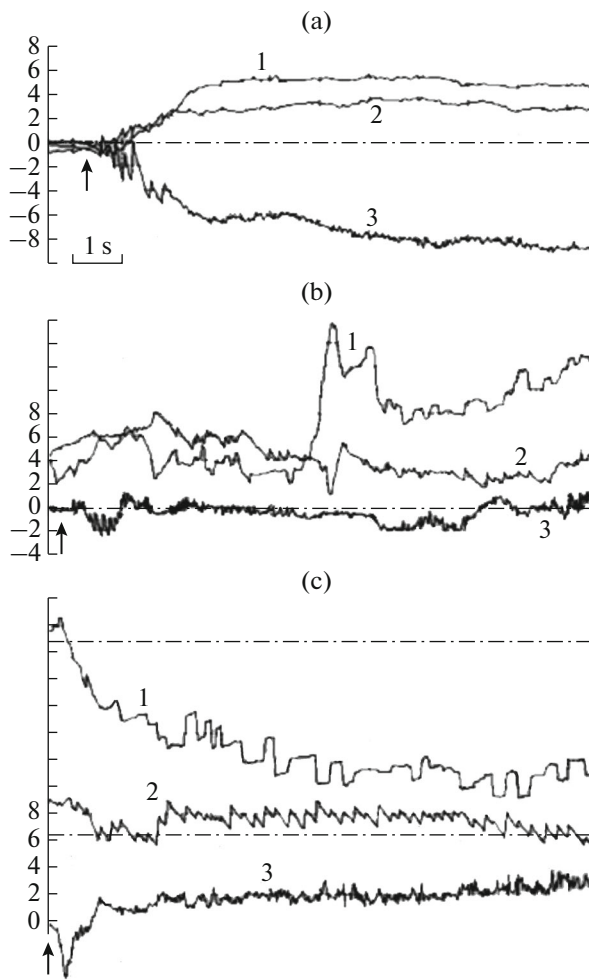
Comparative analysis of groups 1 and 2 showed that the most pronounced changes in SEM were observed in the cosmonauts from group 1 since days 1–2 after the flight to days 8–9 and, in a number of cases, to days 13–14. In the cosmonauts from group 2, SEM returned to the background data on days 4–5 after the SF.

The native curves that illustrate SEM before and after the SF were presented earlier [1–3].

*Static Torsion Otolith-Cervico-Ocular Reflex*

Before the SF, the amplitude of compensatory eyeball counter-rotation was within the physiological norm of 4°–8°. The reflex was symmetrical, with the exception of cosmonaut 1, who had a counter-rotation angle of 4° and 7° when inclining the head to the left and to the right, respectively.

In group 1 on days 1 and 2 after the SF, 33% of the cosmonauts were not observed to have OCOR (the absence of compensatory torsion eyeball counter-rotation), 22% had an inversion of OCOR (the torsion eyeball rotation during inclining the head to the shoulder was directed towards the head inclination), and the remaining 45% had a significant decrease in the amplitude of eyeball counter-rotation by a factor of 2–2.5. In group 1, OCOR was not observed to be within the norm on day 1–2 after the SF.



**Fig. 1.** OCOR before and two days after the SF: (a) before the SF; (b) after the SF (the absence of OCOR); (c) after the SF (the inversion of OCOR). 1, Horizontal VOG; 2, vertical VOG; 3, torsional VOG; ↑, the moment of head inclination.

On day 4–5 after the flight, OCOR was normal in 45% of the cosmonauts from group 1, and 55% had a lowered OCOR. On day 8–9 after the flight, OCOR was normal in 72% of the cosmonauts from group 1, and 28% of the cosmonauts had a lowered OCOR until days 13–14 after the SF.

In group 2 on day 1–2 after the SF, 29% of the cosmonauts had a normal OCOR (without significant differences from the background), 64% had a significant decrease in the amplitude of eyeball counter-rotation, and the remaining 7% had no OCOR.

On days 4–5 after the flight, OCOR was normal in 79% of the cosmonauts from group 2, and 21% had a lowered OCOR. On days 8–9 after the flight, OCOR was normal in all cosmonauts from group 2.

Consequently, the atypical form of OCOR (the inversion or absence of compensatory torsion eyeball counter-rotation, Fig. 1) on days 1–2 after the flight

was typical of the cosmonauts from group 1 who had no prior SF experience.

Quantitative analysis of post-flight changes in OCOR was made using the gain factor (gfOCOR), for which the dynamics of post-flight changes is presented in Fig. 2.

The performed statistical analysis revealed a significant decrease in the gfOCOR in group 1 on days 1–2 and 4–5 after the SF in comparison with both the background and data for days 8–9.

In group 2, a significant decrease in the gfOCOR was observed only on days 1–2 after the SF.

Comparative analysis of the coefficient of variation (CV) in the gfOCOR in groups 1 and 2 showed that the scatter of the gfOCOR parameter in group 2 was 1.5–2 times smaller than in group 1. A significant growth in the CV gfOCOR after the SF was observed in both groups until days 8–9 after the SF, which indicates the high post-flight variability of the amplitude of compensatory torsion counter-rotation.

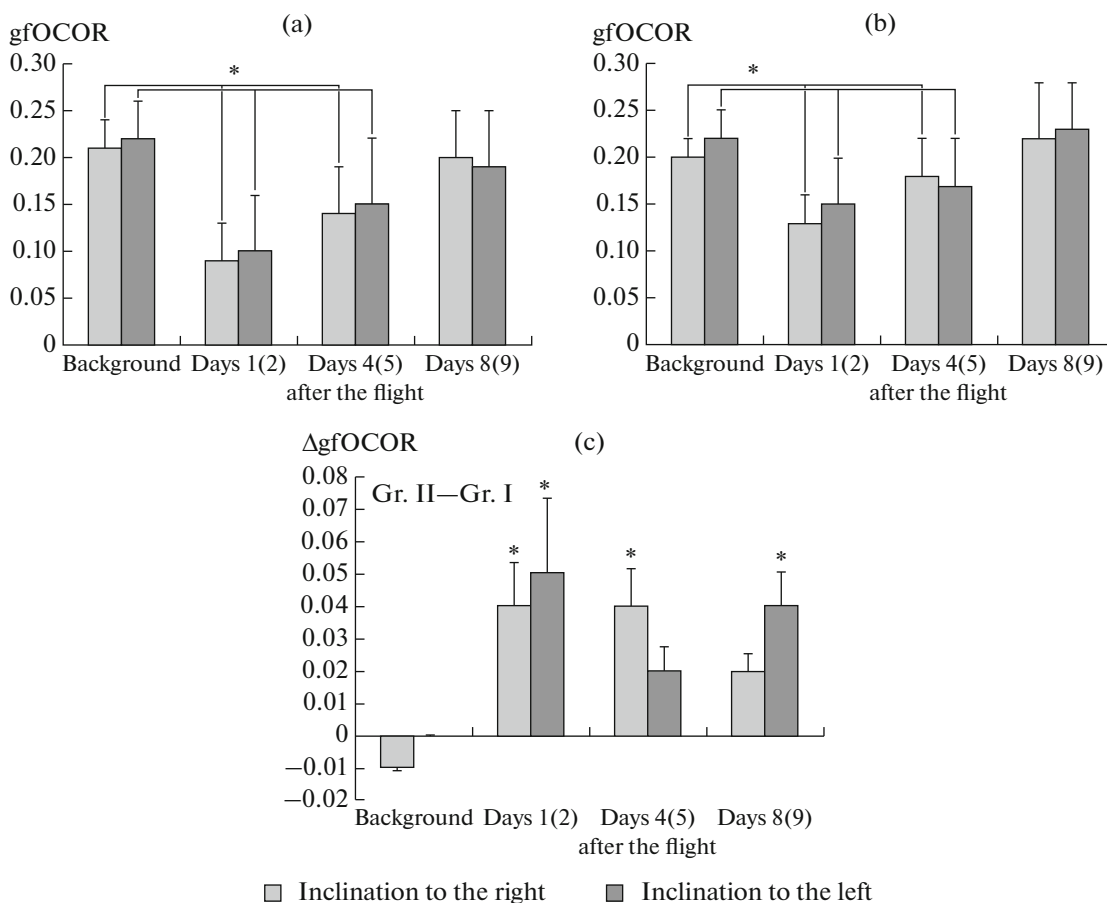
Figure 2 also presents the difference between the gfOCOR in groups 1 and 2 ( $\Delta$ gfOCOR), which shows the difference in the processes of post-flight OCOR re-adaptation in the absence and presence of prior SF experience.

As the figure shows,  $\Delta$ gfOCOR is within 0.02–0.05 since days 1–2 after the SF until days 8–9. This means that the cosmonauts from group 2 were observed to have the compensatory torsion eyeball counter-rotation with the amplitude that was on average  $\sim 1^\circ$  higher than the amplitude in group 1. The inter-group comparison of the gfOCOR (the Mann–Whitney test) showed that there were significant differences between the gfOCOR in groups 1 and 2 until days 8–9 after the SF.

#### *The Dynamic Vestibular-Cervico-Ocular Reflex and Vestibular Reactivity*

The post-flight changes in VCOR were analyzed using the gain factor (gfVCOR). Before the flight, the gfVCOR was within the physiological norm of 0.4–0.5 in all the cosmonauts.

After the SF, the cosmonauts from group 1 were divided into two subgroups according to the nature of the gfVCOR. In the first subgroup (39% of the cosmonauts), the gfVCOR sharply grew to 0.7–0.8 since days 1–2 after the flight. The increase in the gfVCOR was caused either by the decrease in the speed of head rotation along the longitudinal axis of the body, or by the increase in the speed of eyeball counter-rotation. In the second subgroup (61% of the cosmonauts), the gfVCOR was sharply reduced to 0.1–0.15 or was almost zero due to the absence of the compensatory eyeball counter-rotation reflex. The significant changes in the gfVCOR in both subgroups of group 1 were observed until days 8–9 after the SF.



**Fig. 2.** gFOCOR before and after the SF: (a) group 1; (b) group 2; (c) the difference between groups 1 and 2 ( $\Delta$ gFOCOR); \* marks significant difference from the background,  $p < 0.05$ .

The gFOCOR was normal in 78% of the cosmonauts from group 2 since days 1–2, with the exception of two cosmonauts in whom this parameter was slightly elevated, and one cosmonaut in whom it was lowered.

An analysis of the coefficient of variation (CV) in the gFOCOR showed that the significant growth in the variability of the gFOCOR was observed in both groups until days 8–9 after the SF. Meanwhile, the most pronounced growth in the CV after the SF is observed in the cosmonauts from group 1 with a lowered gFOCOR.

The dynamics of post-flight changes in the gFOCOR in groups 1 and 2 are presented in Fig. 3.

Vestibular reactivity (VR) was assessed according to the nature, intensity, and quantitative indices of the nystagmus that overlaps the compensatory eyeball counter-rotation reflex during the test for studying the VCOR.

Figure 4 shows fragments of the native curves during head rotation before and two days after the SF in three cosmonauts of both groups. Pronounced nystagmus was recorded both against the background of compensatory eyeball counter-rotation (cosmonauts

K1 and K3) and in the case where eyeball counter-rotation was almost absent (cosmonaut K2).

Before the SF, active head rotations were accompanied by a single nystagmus in only 9% of all the examined cosmonauts (two from group 1 and one from group 2), while the other cosmonauts had no nystagmus.

The indicators of the vestibularly induced nystagmus that overlaps the compensatory eyeball counter-rotation reflex during the test for studying the VR and VCOR are presented in Table 3.

In group 1, 83% of the cosmonauts on days 1–2 after the SF, 50% on days 4–5, and 11% on days 8–9 were recorded to have an intensified vestibularly induced nystagmus ( $T_{Ny} \sim 30\text{--}50\%$ ,  $F_{Ny} \sim 3\text{ Hz}$ ,  $A_{Ny} \sim 9^\circ\text{--}11^\circ$ ,  $V_{Ny} \sim 12\text{--}16^\circ/\text{s}$ ), the direction of which depended on the direction of head movement. The nystagmus was recorded both in the presence of the normal VCOR and against the background of an abrupt decrease in the amplitude of compensatory eyeball counter-rotation. An intensified VR and significant changes in the indices of the vestibular nystagmus were observed in these cosmonauts until

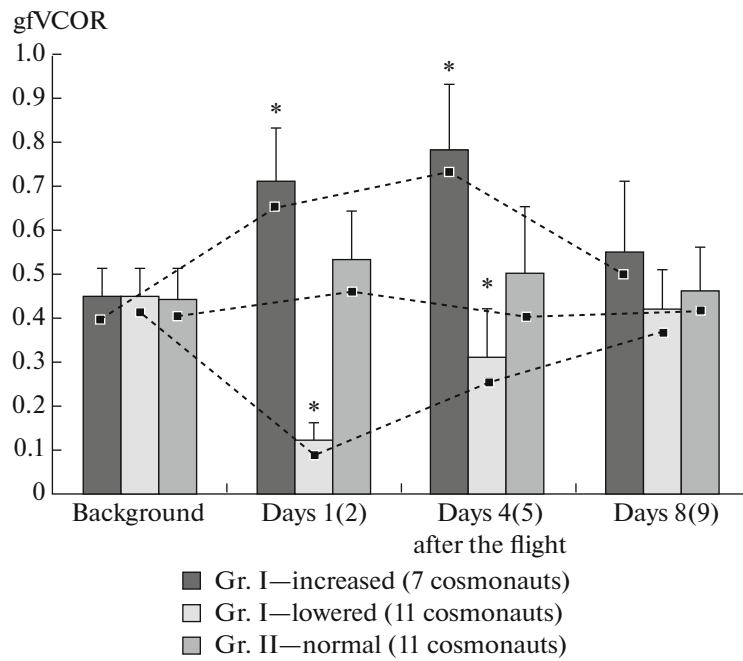


Fig. 3. gVCOR before and after the SF. □ The median of the sample; \* significant difference from the background,  $p < 0.05$ .

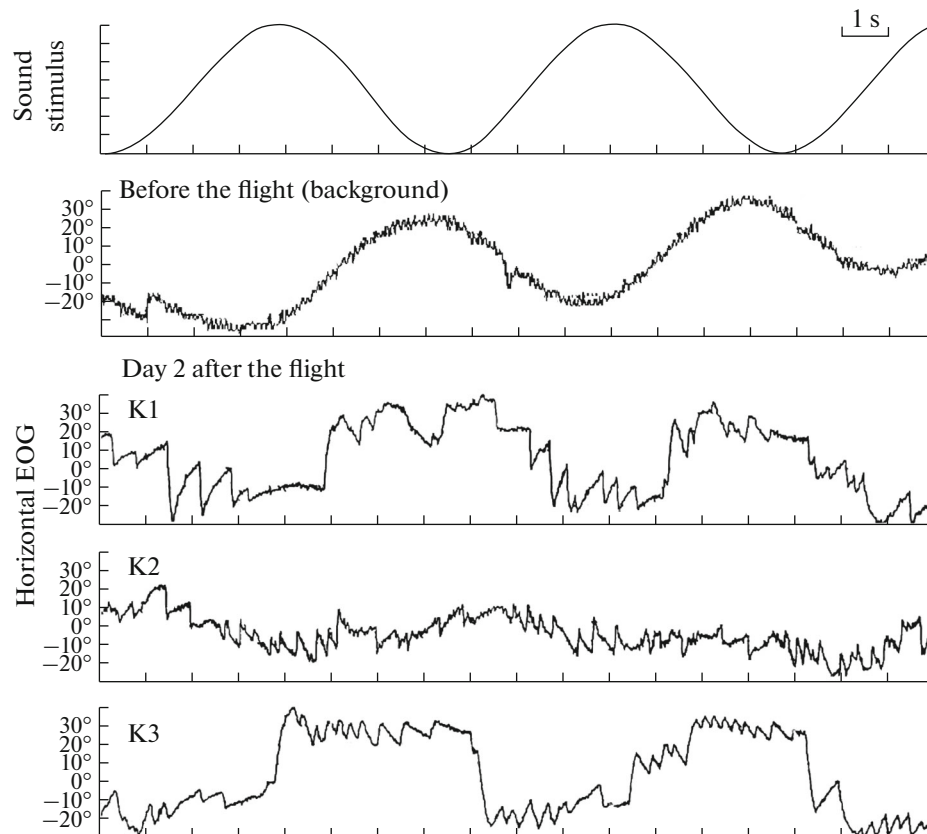


Fig. 4. VCOR and VR before and after the SF. The abscissa axis ( $X$ ), the time of the test, seconds; the ordinate axis ( $Y$ ), the horizontal EOG, degrees.

**Table 3.** Parameters of the vestibular nystagmus before and after the SF

Nystagmic parameter	Background	Day 1 after the SF	Days 4–5 after the SF	Days 8–9 after the SF
	$M \pm \sigma$ CV	$M \pm \sigma$ CV	$M \pm \sigma$ CV	$M \pm \sigma$ CV
Group 1 (nystagmus in 15 cosmonauts on days 1–2, in 9 cosmonauts on days 4–5, and in 2 cosmonauts on days 8–9)				
Relative duration ( $T_{Ny}$ ), %	No nystagmus	47.3 ± 10.1* ↑ 21.4% * ↑	32.9 ± 12.2* ↓ 37.1% ↑	25.6 ± 14.3 55.9%
Frequency, ( $F_{Ny}$ ), Hz		3.2 ± 0.6* 18.8% * ↑	2.9 ± 0.7* 24.1% *	3.0 ± 0.9 30.0%
Amplitude of the rapid phase ( $A_{Ny}$ ), degrees		11.1 ± 3.4* 30.6% * ↑	9.4 ± 2.8* 29.8% *	8.7 ± 4.1 47.1%
Speed of the slow phase ( $V_{Ny}$ ), °/s		15.6 ± 7.0* 44.9% * ↑	12.4 ± 8.3* 66.9% * ↑	13.6 ± 6.0 44.1%
Group 2 (nystagmus in four cosmonauts)				
Relative duration ( $T_{Ny}$ ), %	No nystagmus	28.3 ± 7.6* ↑ 26.9% * ↑	19.1 ± 5.4* 28.3% *	No nystagmus
Frequency, ( $F_{Ny}$ ), Hz		2.8 ± 0.5* ↑ 17.9% * ↑	3.1 ± 0.8* 25.8% *	
Amplitude of the rapid phase ( $A_{Ny}$ ), degrees		10.0 ± 4.1* ↑ 41.0% * ↑	11.9 ± 3.7* 31.1% *	
Speed of the slow phase ( $V_{Ny}$ ), °/s		11.7 ± 5.6 ↑ 47.9% * ↑	13.1 ± 6.2* 47.3% *	

\* Significant difference from the background and data on days 8–9,  $p < 0.05$ ; ↑ or ↓ significant difference (increase or decrease) in comparison with the previous section,  $p < 0.05$ .

days 8–9. In the remaining cosmonauts of group 1, VR corresponded to the background, and the nystagmus was almost absent.

In group 2, 28% of the cosmonauts were observed to have an intensified VR and pronounced nystagmus on days 1–2 and 4–5 after the SF with the normalization of VR on days 8–9. In the remaining cosmonauts, VR corresponded to the background during the entire post-flight period.

Although the frequency of nystagmus and its amplitude and speed indices on days 1–2 and 4–5 after the SF were almost the same in the cosmonauts from groups 1 and 2, the relative duration of nystagmus  $T_{Ny}$  in group 1 was 1.5–2 times higher in comparison with group 2.

In addition to the statistical analysis of the reliability of differences in the studied parameters before and after the SF, the correlation analysis was also performed to determine the presence or absence of direct (linear) relationships between the re-adaptive changes in the indicators of the state of individual levels of the vestibular system.

The cosmonauts from group 1 had a negative correlation between the parameters OCOR and VCOR/VR (vestibular nystagmus) since days 1–2 after the SF until days 8–9 ( $r = -0.6$  to  $-0.8$ ;  $p < 0.05$ ).

Thus, the analysis and comparison of groups 1 and 2 made it possible to estimate the impact of repeated SFs and to detect a number of statistically significant post-flight changes in the studied parameters, which were not found when analyzing the common group.

The significant improvement in the parameters of the vestibular function and reduction in the time spent on their post-flight recovery in the cosmonauts who have a preliminary SF experience can be explained as follows.

In vestibular physiology, there is a well-known phenomenon called *attenuation* (in Russian literature, it is customary to use the term *adaptation*) [7, 8]. The description of the attenuation of the vestibular reflexes, especially the vestibular nystagmus, has been the subject of many researches. The attenuation of the nystagmus has been described in humans, monkey, cat, rabbit, and pigeon [7, 8]. This reaction depends on the central mechanisms, the location of which is not yet known, although there are opinions that the cerebellum, cortex, and trunk formations may be responsible for the attenuation [9]. The inhibition of the vestibular reflexes (nystagmus) is interpreted as a consequence of the central inhibition of oculomotor reactions that is caused by the disturbance in the rela-

tionship of the afferent systems that are involved in the implementation of the vestibular reactions [10].

Thus, significant differences in vestibular reflexes in the cosmonaut groups with the presence and absence of preliminary space flight experience and reduction in the time of their post-flight recovery can be explained by the phenomenon of “adaptation”.

### CONCLUSIONS

Repeated stay in the long-term SF leads to the abrupt, statistically significant reduction in the period of re-adaptation of the vestibular function.

After the flight, the cosmonauts from group 1 (who were in the long SF for the first time) are observed to experience the following re-adaptation changes:

—Increase in the reactivity of the semicircular ducts of the vestibular entry.

—Decrease in the level of tonic (static) vestibular excitability.

—Atypical disturbances of the vestibular function (the inversion or absence of OCOR, the absence of VCOR).

—Change in the nature of interaction between the otoliths and semicircular ducts (the inhibition of the otolithic function is accompanied by the increase in the dynamic reactivity of the vestibular system with a negative correlation between the investigated parameters:  $r = -0.6$  to  $-0.8$ ;  $p < 0.05$ ).

In the cosmonauts from group 2 (who had a preliminary experience of long stay in microgravity), significant changes in the state of the vestibular function are observed only on days 1–2 after the SF.

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