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BIOCHEMISTRY, BIOPHYSICS, AND MOLECULAR BIOLOGY

Biochemical Adaptation and Telomere Shortening in Javanese Macaques in Response to Social Isolation

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Abstract—In this study, we examined changes in hormonal status, oxidative status, antioxidant defense, and peripheral blood leukocyte telomere length in male Javanese macaques (*Macaca fascicularis*) following transfer from group housing to individual cages as a model of social isolation. The study was performed in ten male Javanese macaques aged 11–17 years using a longitudinal design: the parameters were assessed in the same animals before transfer to individual cages and after 60 days of isolation. Malondialdehyde (MDA) concentration, superoxide dismutase (SOD) and catalase activities, cortisol, testosterone, and thyroglobulin levels, as well as absolute mean telomere length, were measured. A statistically significant decrease in telomere length ($p = 0.0062$), MDA concentration, and catalase activity ($p < 0.01$), as well as an increase in SOD activity and cortisol level ($p < 0.05$), was observed. Testosterone showed a decreasing trend, whereas thyroglobulin showed an increasing trend. The obtained data indicate systemic changes in the studied parameters in response to isolation. Changes in telomere length and oxidative status may reflect the involvement of mechanisms related to DNA damage and antioxidant system function. The results are consistent with the concept of stages of the general adaptation syndrome.

Keywords: social isolation, telomere length, oxidative stress, antioxidant system, cortisol, macaques

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INTRODUCTION

Exposure to stressors is accompanied by changes in neuroendocrine regulation, including activation of the hypothalamic–pituitary–adrenal axis (HPA) and changes in glucocorticoid signaling [1, 2]. Chronic stress exposure is considered one of the factors capable of causing long-term restructuring of physiological and metabolic processes, including changes in energy metabolism, immune regulation, and redox balance [1, 2].

At the cellular level, chronic stress can be accompanied by DNA damage, changes in the activity of the antioxidant system, and telomere shortening [3–5]. Current understanding of stress-associated changes in telomere length suggests the involvement of several interconnected mechanisms, including changes in glucocorticoid regulation and disruption of the cellular redox balance [4]. In particular, it has been shown that exposure to cortisol can be accompanied by a decrease in telomerase activity in cultured human T-lymphocytes [6]. Oxidative stress is also considered as one of the possible mechanisms of telomere shortening; however, in vivo data remain ambiguous and depend on the experimental model used [3–5].

Social factors in primates are tightly associated with the HPA axis activity. Cortisol levels depend on the nature of social interactions, social rank, frequency of stressful events, and the presence of social support [7]. Because primates are highly social animals, disruption of the habitual social structure, including transfer from group housing to individual cages, can be considered a significant chronic stressor. Therefore, models of social isolation in laboratory primates are of particular interest for studying the physiological and molecular mechanisms of the stress response [8].

When studying stress response models in laboratory primates, the primary focus is typically made on behavioral, neuroendocrine, and physiological indices [8]. The inclusion of molecular markers reflecting genomic stability allows the assessment of adaptive processes to be supplemented with cellular-level indices. In particular, changes in telomere length are considered one of the integral molecular indices of stress-induced changes [4].

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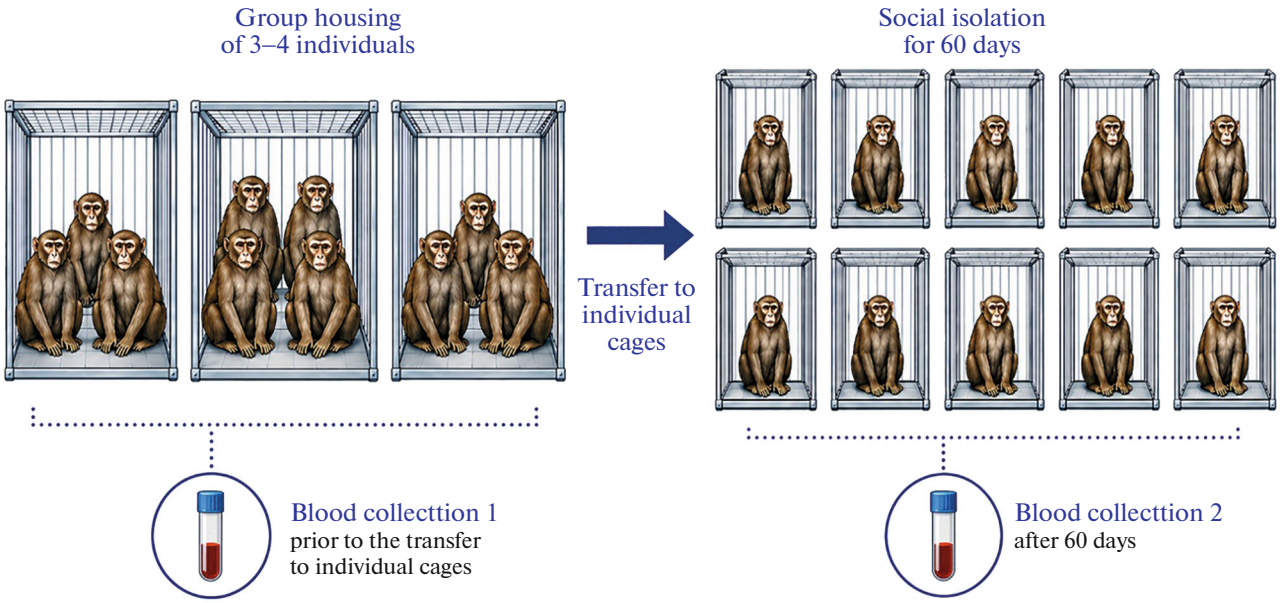


Fig. 1. Experimental design.

Of particular interest is a comprehensive analysis of biomarkers, including hormonal indices, oxidative status parameters, and molecular characteristics, because this approach allows the assessment of adaptive processes at various levels of organization (from systemic to cellular one). This is especially important when studying chronic stress, which is accompanied by long-term reorganization of the body's regulatory mechanisms.

In recent years, the interest of researchers in studying the effects of stress under conditions of isolation and confined space steadily increases, which is associated, in particular, with the tasks of biomedical support for long-term space missions [9]. Under such conditions, social isolation, limited space, environmental depletion, and changes in locomotor activity can have a significant impact on neuroendocrine regulation and the metabolic state of the body [9]. In this regard, laboratory primate models are considered significant for assessing the biological effects of spaceflight factors and increasing the translational value of research [10].

The aim of this study was to identify and characterize the changes occurring in leukocyte telomere length, oxidative status, and hormonal profile in Javanese macaques under conditions of social isolation.

MATERIALS AND METHODS

The study was performed in ten male Javanese macaques (*Macaca fascicularis*) aged 11–17 years. All animals were housed at the animal facility of the Kurchatov Complex for Medical Primatology at the Kurchatov Institute National Research Center. Prior to the experiments, the male Javanese macaques were housed in stable social groups of three or four individuals, providing them with a structured and predictable social environment. The animals were housed in open-air enclosures with access to insulated indoor spaces. Then, the animals were transferred to isolation conditions by placing them to individual cages. Animals previously housed in shared groups were housed in separate rooms, preventing visual contact between familiar individuals (Fig. 1). Diet remained standard throughout the experiment and included compound feed, as well as fresh vegetables and fruits.

A longitudinal design was used, in which parameters were determined in the same animals before their transfer from group housing to individual cages and after 60 days of social isolation.

This approach allowed us to minimize the influence of interindividual variability, increase the sensitivity of detecting stress-induced changes, and ensure a more correct interpretation of the observed shifts as a consequence of the effects of isolation.

In this study, we used blood samples collected before and 60 days after the transfer to isolation conditions. Blood was collected in the morning (9:00–10:00 a.m.) before feeding, without sedation. Samples were collected in tubes containing a coagulation activator to obtain serum and with the anticoagulant K2EDTA to isolate cellular fractions.

The peripheral blood leukocyte telomere length was determined by quantitative real-time PCR according to the O'Callaghan and Fenech protocol [11]. The method is based on the quantitative determination of telomeric repeats and the single-copy gene, followed by calculation of the absolute mean telomere

length in kilobase pairs (kb) in the sample. Genomic DNA isolated from peripheral blood leukocytes was used for the analysis. The concentration and quality of the isolated DNA were assessed spectrophotometrically; DNA integrity was controlled by agarose gel electrophoresis. Samples that had no signs of degradation were included in the analysis. Amplification of telomere repeats and the single-copy gene was performed in separate reactions. Telomere length was calculated using standard curves constructed from serial dilutions of synthetic telomeric sequence standards and the single-copy *36B4* gene. All samples were analyzed in technical replicates using negative controls.

Serum MDA concentration was determined by high-performance liquid chromatography after derivatization with thiobarbituric acid. SOD activity was assessed by its ability to inhibit adrenaline autooxidation [12], and catalase activity by the rate of hydrogen peroxide decomposition [13].

The levels of cortisol, testosterone, and thyroglobulin were determined by enzyme immunoassay using the Cortisol-IMAXYZ, Testosterone-IMAXYZ and TG-IMAXYZ kits manufactured by Vital Development Corporation (Russia) according to the manufacturer's instructions.

Data were statistically processed using nonparametric methods. The distribution normality was assessed using the Shapiro–Wilk test. Differences between the baseline and post-isolation states were assessed using the Wilcoxon signed-rank test for related samples. Correlation analysis with Spearman's rank correlation coefficient was used to analyze correlations between parameters. Individual changes in parameters (Δ) were additionally calculated for each animal. These changes represent the difference between the baseline and post-isolation values. This approach allowed us to assess the direction and severity of intra-individual changes and use them in analyzing correlations between parameters.

RESULTS AND DISCUSSION

The results of the study, reflecting changes in telomere length, oxidative status indices, and hormonal profile in Javanese macaques during social isolation, are presented in Fig. 2.

Under social isolation conditions, a statistically significant decrease in leukocyte telomere length compared to baseline ($p = 0.0062$; Fig. 2a) was observed in Javanese macaques. The median telomere length decreased from 18.83 to 13.70 kb. This decrease was observed in the majority of animals, indicating a systematic nature of the observed changes.

Taking into account the longitudinal design of the study, these changes should be interpreted as changes in the index relative to the baseline level in the same animals, rather than as a manifestation of interindividual variability. Importantly, telomere shortening was recorded over a relatively short observation period (60 days), which may indicate the high sensitivity of this index to changes in environmental conditions. The observed changes should be considered a molecular response to stress rather than a direct evidence of pronounced cellular aging.

Changes in oxidative status parameters were characterized by a decrease in MDA concentration (Fig. 2b) and catalase activity (Fig. 2d) ($p < 0.01$) with a simultaneous increase in SOD activity (Fig. 2c) ($p < 0.05$). The median MDA concentration decreased from 3.598 to 1.060 μmol/L, the median SOD activity increased from 1296.616 to 1918.275 U/min/g Hb, and the median catalase activity decreased from 0.095 to 0.065 H_2O_2/min/g Hb.

This combination of changes may reflect rearrangement of the enzymatic component of the antioxidant system due to changes in the intensity of lipid peroxidation processes. An increase in the activity of SOD, which catalyzes the dismutation of the superoxide radical to form hydrogen peroxide, against a background of decreased activity of catalase, which is involved in its degradation, may indicate an unbalanced change in individual components of the antioxidant defense system. Given the known concepts of the role of oxidative stress in damaging cellular structures and shortening telomeres, such changes may be important for interpreting the observed telomere shortening [3, 5].

A decrease in MDA concentration with a simultaneous increase in SOD activity should not be interpreted as just an increase in oxidative damage. It is more accurate to view this profile as a sign of an adaptive restructuring of the redox balance, in which a decrease in one of the end products of lipid peroxidation is combined with a change in the activity of antioxidant enzymes. Taken together, the observed profile of changes may indicate a compensatory reorganization of the antioxidant system with signs of imbalance in its individual components.

In terms of hormonal regulation, an increase in cortisol levels was detected ($p < 0.05$; Fig. 2e): the median value increased from 457.45 to 813.36 nmol/L. For testosterone, a tendency towards a decrease in the median from 20.06 to 12.26 nmol/L was noted (Fig. 2f); for thyroglobulin, a tendency towards an increase from 20.03 to 24.76 ng/ml (Fig. 2g). These data may indicate that the hormonal response to stress is not limited to the activation of the HPA axis, but may also affect gonadal and thyroid regulation.

The identified changes in the hormonal profile should be considered in the context of the complex stress response. Increased cortisol levels reflect the involvement of glucocorticosteroids in the systemic adaptive response, including the regulation of energy metabolism and the redistribution of physiological resources during stress [1, 2]. The tendency toward decreased testosterone levels may be associated with

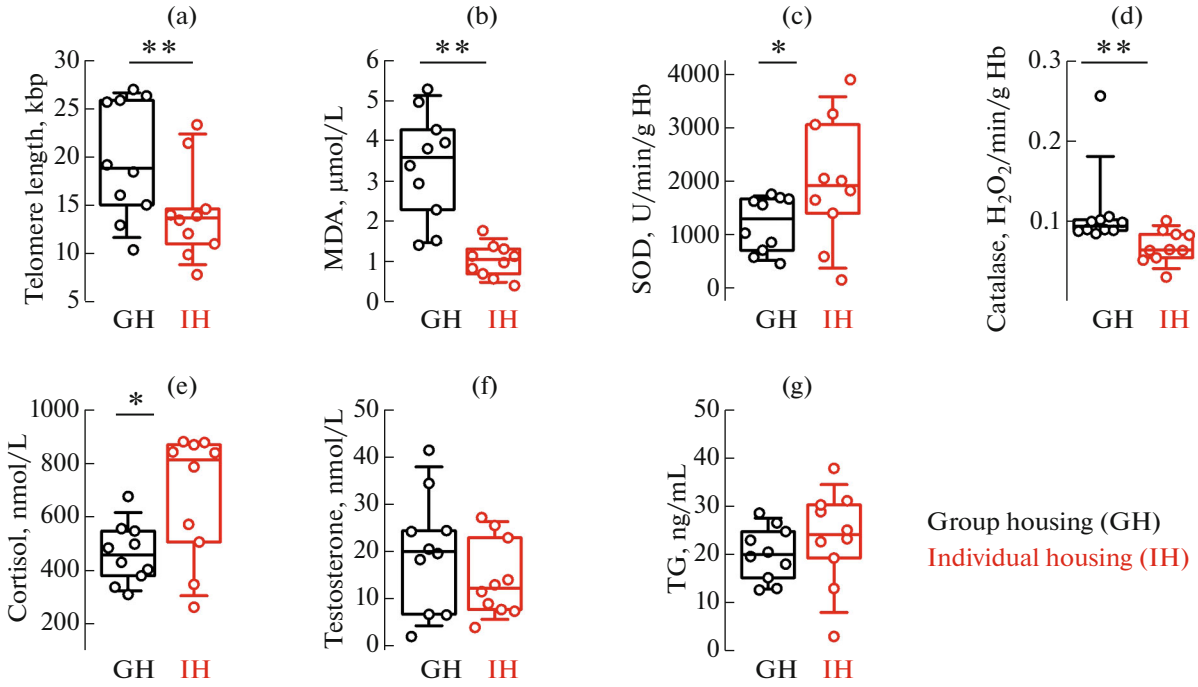


Fig. 2. Changes in the studied parameters in Javanese macaques during group housing (GH) and after 60 days following transfer to individual cages (IH): (a) peripheral blood leukocyte telomere length, kbp; (b) malondialdehyde (MDA) concentration, μmol/L; (c) superoxide dismutase (SOD) activity, U/min/g Hb; (d) catalase activity, H_2O_2/min/g Hb; (e) cortisol concentration, nmol/L; (f) testosterone concentration, nmol/L; (g) thyroglobulin (TG) concentration, ng/mL. The plots show individual values, median, and interquartile range (Q1–Q3). Statistical significance of differences was assessed using the Wilcoxon signed-rank test: $*p < 0.05$; $**p < 0.01$.

the inhibitory effect of stress-induced glucocorticosteroid signaling on the hypothalamic–pituitary–gonadal axis [14].

The performed correlation analysis revealed a positive correlation between the MDA concentration and catalase activity in animals after 60 days of isolation ($rs = 0.803$; $p < 0.01$), which may reflect the correlation between the intensity of lipid peroxidation and the activity of antioxidant defense. When analyzing individual changes in the parameters, tendencies towards a negative correlation between the change in telomere length and the change in MDA concentration ($rs \approx -0.60$), as well as between the change in telomere length and the change in catalase activity ($rs \approx -0.66$), were noted. In addition, a tendency towards an association between the change in telomere length and the change in testosterone level was observed ($rs \approx -0.58$). The correlations between changes in telomere length and changes in SOD activity and cortisol and thyroglobulin levels were not statistically significant. Given the limited sample size, these correlations are preliminary and require confirmation in studies in larger groups of animals.

CONCLUSIONS

The data obtained indicate the formation of a coordinated adaptive response, including changes in the hormonal profile, oxidative status, and telomere length in Javanese macaques after 60 days of social isolation. Increased cortisol levels are consistent with activation of the HPA axis and the involvement of glucocorticosteroids in the systemic stress response [1, 2]. Changes in the antioxidant system, including an increase in SOD activity along with a decrease in catalase activity and MDA concentrations, may indicate a compensatory reorganization of the redox balance with signs of functional stress on individual components of the antioxidant defense system.

Telomere shortening, identified in the longitudinal design, should be considered a molecular marker of the response to stress, potentially associated with changes in the redox balance and regulation of cellular homeostasis [3–5]. Unlike a number of biochemical indices reflecting the current functional state, telomere length can be considered an integral molecular index of cell state associated with mechanisms maintaining genomic stability [4].

Taken together, the observed changes indicate the involvement of the mechanisms that ensure adaptation to prolonged stress and the maintenance of cellular homeostasis under changing environmental conditions. The obtained profile of changes can be interpreted in the context of the resistance stage of general adaptation syndrome, in which functional equilibrium

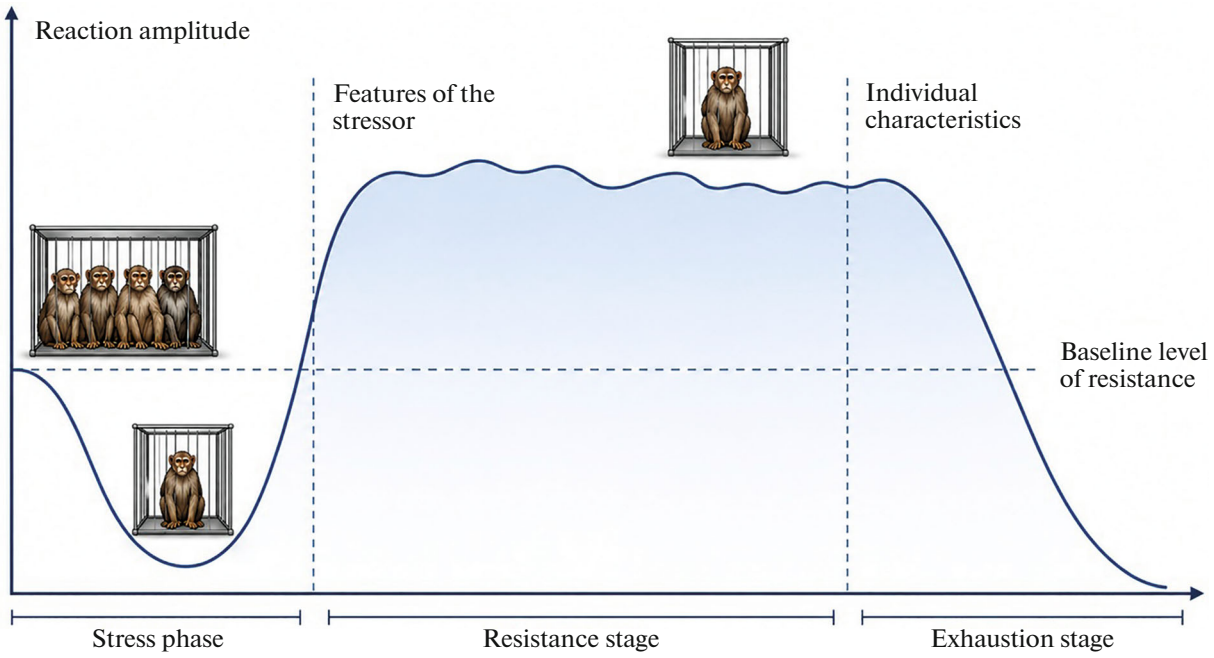


Fig. 3. Schematic representation of the adaptive response to social isolation in the context of the general adaptation syndrome.

is maintained through the activation of compensatory systems [15] (Fig. 3).

The use of a longitudinal design allowed us to increase the sensitivity in identifying stress-induced changes and the accuracy of their interpretation. However, the limited sample size, typical of studies involving laboratory primates, remains a significant limitation of such models and may reduce the statistical power of analysis for certain indices [8].

The obtained results highlight the importance of an integrated approach combining hormonal, biochemical, and molecular indices for assessing adaptation processes under chronic stress.

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AUTHOR CONTRIBUTION

O.P. Chzhu, M.F. Timina, A.V. Popov—study concept and supervision; O.P. Chzhu, M.F. Timina, R.M. Kirgintsev, N.S. Rudenko, Y.Y. Bondareva—experiments; O.P. Chzhu, M.F. Timina—data analysis and interpretation; O.P. Chzhu, M.F. Timina, N.S. Rudenko—preparation and editing of the article; O.P. Chzhu, M.F. Timina—discussion of the results; M.F. Timina—revision of the manuscript and preparation of responses to the reviewers' comments.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Animal experiments were conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals (http://oacu.od.nih.gov/regs/index.htm). The study protocol was approved by the local biomedical research ethics committee of the National Research Center "Kurchatov Institute" (protocol no. 02-3 dated May 28, 2025).

CONFLICT OF INTEREST

The authors of this work declare that they have no conflicts of interest.

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REFERENCES

1. Lupien, S.J., McEwen, B.S., Gunnar, M.R., and Heim, Ch., Effects of stress throughout the lifespan on the brain, behaviour and cognition, *Nat. Rev. Neurosci.*, 2009, vol. 10, no. 6, pp. 434–445. https://doi.org/10.1038/nrn2639
2. Sapolsky, R.M., Romero, L.M., and Munck, A.U., How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions, *Endocr. Rev.*, 2000, vol. 21, no. 1, pp. 55–89. https://doi.org/10.1210/edrv.21.1.0389
3. Von Zglinicki, T., Oxidative stress shortens telomeres, *Trends Biochem. Sci.*, 2002, vol. 27, no. 7, pp. 339–344. https://doi.org/10.1016/s0968-0004(02)02110-2
4. Shalev, I., Entringer, S., Wadhwa, P.D., Wolkowitz, O.M., Puterman, E., Lin, J., and Epel, E.S., Stress and telomere biology: a lifespan perspective, *Psychoneuroendocrinology*, 2013, vol. 38, no. 9, pp. 1835–1842. https://doi.org/10.1016/j.psyneuen.2013.03.010
5. Armstrong, E. and Boonekamp, J., Does oxidative stress shorten telomeres in vivo? A meta-analysis, *Ageing Res. Rev.*, 2023, vol. 85, 101854. https://doi.org/10.1016/j.arr.2023.101854
6. Choi, J., Fauce, S.R., and Effros, R.B., Reduced telomerase activity in human T lymphocytes exposed to cortisol, *Brain, Behavior, and Immunity*, 2008, vol. 22, no. 4, pp. 600–605. https://doi.org/10.1016/j.bbi.2007.12.004
7. Abbott, D.H., Keverne, E.B., Bercovitch, F.B., Shively, C.A., Mendoza, S.P., Saltzman, W., Snowdon, C.T., Ziegler, T.E., Banjevic, M., Garland, T., and Sapolsky, R.M., Are subordinates always stressed? A comparative analysis of rank differences in cortisol levels among primates, *Horm. Behav.*, 2003, vol. 43, no. 1, pp. 67–82. https://doi.org/10.1016/s0018-506x(02)00037-5
8. Meyer, J.S. and Hamel, A.F., Models of stress in nonhuman primates and their relevance for human psychopathology and endocrine dysfunction, *ILAR J.*, 2014, vol. 55, no. 2, pp. 347–360. https://doi.org/10.1093/ilar/ilu023
9. Dunn Rosenberg, J., Jannasch, A., Binsted, K., and Landry, S., Biobehavioral and psychosocial stress changes during three 8–12 month spaceflight analog missions with Mars-like conditions of isolation and confinement, *Front. Physiol.*, 2022, vol. 13, 898841. https://doi.org/10.3389/fphys.2022.898841
10. Desai, R.I., Kangas, B.D., and Limoli, Ch.L., Nonhuman primate models in the study of spaceflight stressors: past contributions and future directions, *Life Sci. Space Res.*, 2021, vol. 30, pp. 9–23. https://doi.org/10.1016/j.lssr.2021.03.008
11. O'Callaghan, N.J. and Fenech, M., A quantitative PCR method for measuring absolute telomere length, *Biol. Proced. Online*, 2011, vol. 13, no. 1, p. 3. https://doi.org/10.1186/1480-9222-13-3
12. Sirota, T.V., A new approach to the study of adrenaline autoxidation and its application for measuring superoxide dismutase activity, *Vopr. Med. Khim.*, 1999, vol. 45, no. 3, pp. 263–272.
13. Korolyuk, M.A., Ivanova, L.I., and Mayorova, I.G., A method for determining catalase activity, *Lab Delo*, 1988, no. 1, pp. 16–19.
14. Whirledge, Sh. and Cidlowski, J.A., A role for glucocorticoids in stress-impaired reproduction: beyond the hypothalamus and pituitary, *Endocrinology*, 2013, vol. 154, no. 12, pp. 4450–4468. https://doi.org/10.1210/en.2013-1652
15. Selye, H., Stress and the general adaptation syndrome, *Br. Med. J.*, 1950, vol. 1, no. 4667, pp. 1383–1392. https://doi.org/10.1136/bmj.1.4667.1383

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