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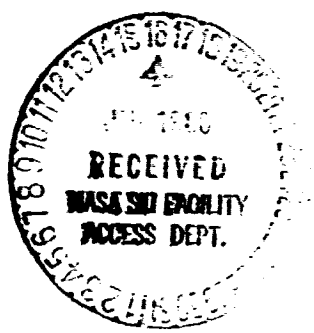
NASA TECHNICAL MEMORANDUM NASA TM-75968

CHANGE IN RADIOSENSITIVITY OF RATS DURING HYPOKINETIC STRESS

I. P. Chernov

Translation of "Izmeniniye radiochuvstvitel'nosti krys v techeniye gipokineticheskogo stress", Radiobiologiya, No. 4 (1978) pp 574-578.



NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON, D. C. 20546 January 1980

STANDARD TITLE PAGE

1. Report No. NASA TM-75968	2. Government Accession No.	3. Recipient's Catalog No.
4. Title and Subtitle: Change in Radiosensitivity of Rats During Hypokinetic Stress		5. Report Date: January, 1980
		6. Performing Organization Code
7. Author(s): I. P. Chernov		8. Performing Organization Report No.
		10. Work Unit No.
9. Performing Organization Name and Address: SCITRAN, Box 5456, Santa Barbara, CA 93108		11. Contract or Grant No. NASw-3198
		13. Type of Report and Period Covered: Translation
12. Sponsoring Agency Name and Address: National Aeronautics and Space Administration, Washington, D.C. 20546		14. Sponsoring Agency Code

15. Supplementary Notes

Translation of "Izmeninive radiochuvstvitel'nosti krys v techeniye gipokineticheskogo stressa", Radiobiologiya, No. 4, 1978, pp 574-578.

16. Abstract

γ-irradiation (800 rad) of rats on the third day of exposure to hypokinesia increase the radiosensitivity of the animals which was determined by the survival rate and the dynamics of body weight and the weight of some internal organs. The same radiation dose was given on the 20th day of hypokinesia and on the third day of recovery from the 20-day hypokinesia decreased the radiosensitivity of rats. The variations in the radiosensitivity observed may be due to a stress effect of hypokinesia.

17. Key Words (Selected by Author(s))	18. Distribution Statement
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19. Security Classif. (of this report)	20. Security Classif. (of this page)	21. No. of Pages	22. Price
Unclassified	Unclassified	10	

TITLE SHEET

TRANSLATOR	MIRA S. SHEERBAUM
DATE	JANUARY 9, 1980
TR NUMBER	TM-75968
TRANSL. TITLE	Izmeneniye radiochuvstvitel'nosti krys v techeniye gipokineticheskogo stressa
ENGLISH TITLE	Change in Radiosensitivity of Rats during Hypokinetic Stress
AUTHOR	I. P. Chernov
SOURCE	Radiobiologiya, No. 4 (1978)
PAGES	574-578
WORDS	1470

800 rad with γ-quanta Co^{60} on a "Luch" unit with power of dose 65 rad/min.

Based on the data of a number of indices (weight of body, behavioral reactions, weight of a number of internal organs, morphological evaluation) we had previously established the wave-like nature of the changes in the organism under the influence of hypokinesia with the formation in certain periods of resistance in relation to it. The latter made it possible to also select the periods of irradiation. The first group of animals was irradiated on the third day of hypokinesia under conditions of the maximum drop in body weight and stimulation of the hypothalamic-hypophysis-adrenal system (content of 11-hydroxycorticosteroid in the blood plasma 14.83 μg% as compared to 6.3 μg% in intact rats). The second group was irradiated on the 20th day of hypokinesia under conditions of stabilization in body weight and content of 11-Hydroxycorticosteroid on levels close to the initial parameters. The third group was irradiated on the third day of restoration after 20 days of hypokinesia when the phenomena of excitation induced by the release of the animals from the cages had passed. The controls were rats exposed to the effect only of hypokinesia or irradiated without additional effects. The animals of the experimental and control groups were killed by decapitation in 1,3,10, 30 and 45 days after irradiation; for 6 rats for each period a recording was made of the body weight, weight of hypophysis, adrenals, spleen, heart and testicles. The results of the study were processed by the method of variation statistics [4]. The reliability of the differences was evaluated according to Student's criterion (with $D<0.05$).

Results and Discussion

In our experiments hypokinesia induced in rats a stress reaction which was expressed in the characteristic dynamics of weight of the animals, phase changes in the biochemical and histochemical indices of activity of the hypothalamus-hypophysis-adrenal gland system, and reaction of the lymphoid organs. The mobilization period lasted 5-7 days, the period of "chronic resistance" the next 30 days. The survival rate of the rats in this group /575
was 100%. It is apparent from the table that the survival rate of rats

EFFECT OF HYPOKINESIA ON RADIO-SENSITIVITY OF RATS

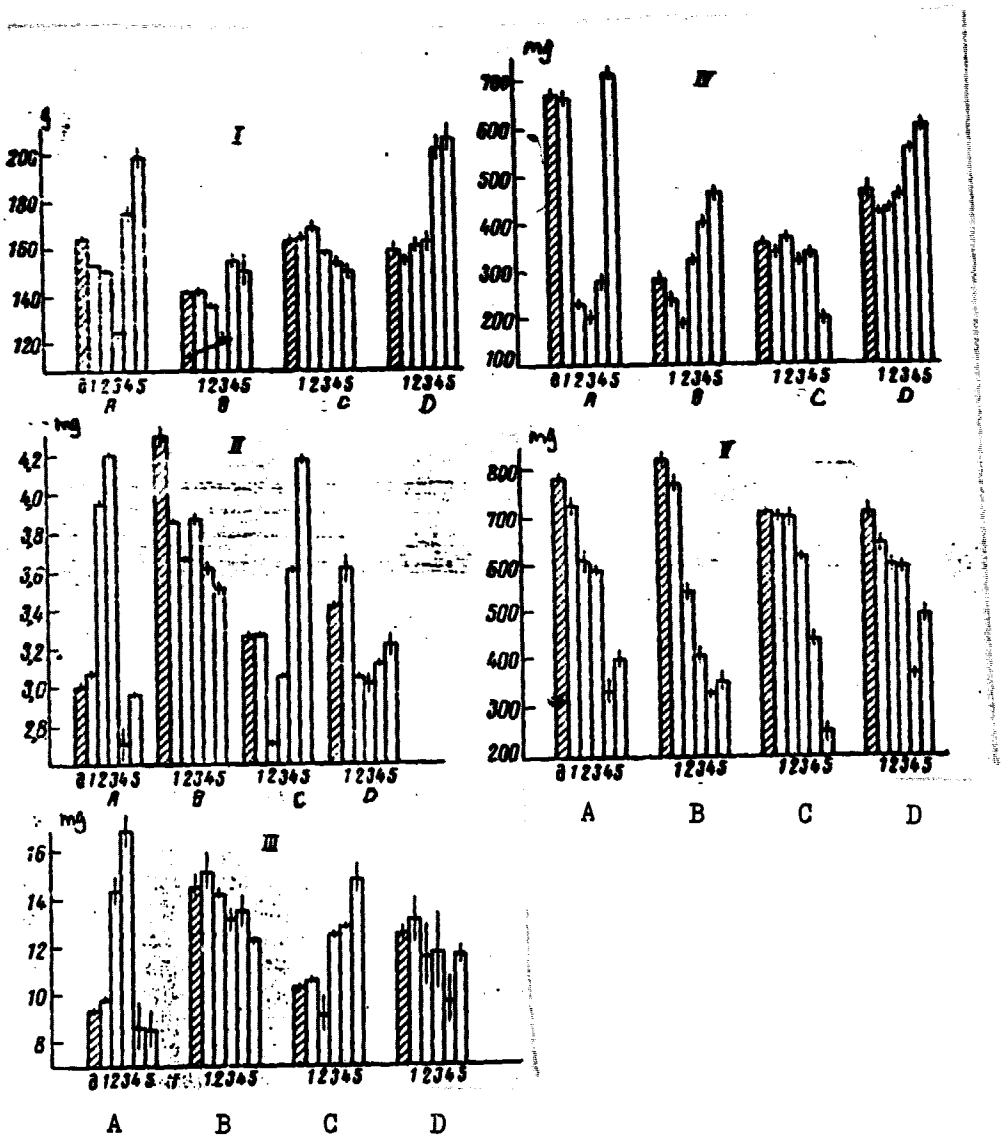
Effect	Survival rate in 45 days, %	D
irradiation without additional effects	30.0±10.1 (20)*	-
irradiation on third day of hypokinesia	19.2±7.9 (26)	0.2
irradiation on 20th day of hypokinesia	75.0±8.2 (28)	0.001
irradiation on third day of restoration after 20 days of hypokinesia	58.3±10.1 (24)	0.02

D--index of importance of difference in survival rate in rats with combined effect and with irradiation without additional effects.

*In parentheses--number of rats in experiment.

irradiated with a dose of 800 rad with subsequent maintenance under normal vivarium conditions by the 45th day was 30%. The death of the irradiated animals occurred in the period of the height of radiation sickness (on the 10th-20th day). In the group of rats irradiated on the third day of isolation and limited mobility the survival rate remained on the level of the control (differences were statistically insignificant), however the death of the animals occurred in earlier periods (on the fifth-tenth day). In the group of rats irradiated on the 20th day of hypokinesia a statistically important increase in the survival rate was observed, while the periods of death of the animals were significantly postponed (35-45th day). The increased survival rate was also maintained in the period of restoration after 20 days of hypokinesia.

Analysis of the change in body weight of the rats also reveals the modifying effect of hypokinesia on the radiation trauma (figure). In rats irradiated without additional effects the weight was reduced, reaching the minimum at the height of the radiation sickness (on the tenth day 125±3.3 g as compared to the initial 164±0.8 g). In the surviving animals the body weight reached the initial level by the 30th day and significantly rose by the 45th day of the experiment. In the group of rats irradiated on the third day under hypokinetic conditions, the weight was reduced already by the moment of irradiation, while the effect of radiation resulted in a



Change in Body Weight (I), Weight of Hypophysis (II), Adrenals (III), Spleen (IV) and Testicles (V) of Rats Irradiated in a Dose of 800 rad under Different Experimental Conditions

A--irradiation without additional effects; B--irradiation on third day of hypokinesia; C--irradiation on 20th day of hypokinesia; D--irradiation on third day of restoration after 20 days of hypokinesia; 1,2,3,4--periods of observation corresponding to 1,3,10,30 and 45th days after irradiation; ∂--indices of weight by moment of irradiation. The amounts of standard error of the mean values are indicated.

further increased in its shortage. In animals irradiated on the 20th day of hypokinesia, the body weight in the first three periods of observation was maintained on the initial level. A reliable decrease in it in this group was noted only on the 30th and 45th days. The weight indices remained close to the initial level in the first 10 days also in the animals irradiated in the period of restoration after 20 days of hypokinesia. In the subsequent periods of observation in the surviving rats of this group the increase in body weight occurred more intensively than in the other series.

Changes in the relative weight of the hypophysis and adrenals (per 100 g of body weight) in different series of the experiment were in an inverse relationship to the body weight. As a rule, the drop in body weight of the rats was accompanied by an increase in the absolute and relative weight of the studied endocrine organs, and vice versa. The most stable increase in the weight of the hypophysis and the adrenals was noted in the animals irradiated on the third day of hypokinesia. The weight of the endocrine organs in rats irradiated in the period of restoration was altered least of all.

It is known that changes in the spleen during acute radiation sickness are reduced to a decrease in the volume and weight of the organ. In our experiments the weight of the spleen in rats irradiated without additional effects was significantly reduced already on the third day of the experiment (235±12.6 mg as compared to 675±12.0 mg in the intact rats). The weight of /576
the spleen remained on approximately the same level on the 10th and 30th days and was restored by the final period of observation. A more pronounced and earlier reduction in the weight of the spleen was found in the group of rats irradiated on the third day of hypokinesia, whereupon the restoration of it did not occur even by the last period of the experiment. In the rats irradiated on the 20th day of hypokinesia the weight of the spleen in the first three periods of observation was altered to a lesser degree, however by the end of the experiment the deficit in weight of the organ was increased. In the rats irradiated in the period of restoration deviations in the relative weight of the spleen from the initial level

were the least, while restoration of it by the end of the experiment was the most complete.

The relative weight of the testicles in 1 day after irradiation was reduced by 6%, on the third day--by 20%, on the tenth day, by 25%. On the 30th and 45th days of the experiment the reduction in weight was already more significant (by 58 and 55% respectively). Under conditions of the combined effect of the factors of hypokinesia and radiation in the early periods the weight of the testicles was reduced more significantly in the rats irradiated on the third day of hypokinesia. Its deficit by the third day was 29%, by the 10th day--47%. In the animals irradiated on the 20th day of hypokinesia the weight of the testicles in the first 10 days was reduced only by 13%. In the subsequent periods the weight of the testicles in the given experimental group was progressively reduced, and by the end of the experiment was the least in the comparable series (by the 45th day it was reduced by 68%). In the group of rats irradiated in the period of restoration after 20 days of hypokinesia the loss of weight on the third day was 14%, on the 10th day--15%, on the 30th day--47% and on the 45th day--30% of the initial level. /577

Analysis of the findings for survival rate of the rats, dynamics of body weight and relative weight of the studied internal organs shows that extreme hypokinesia is a factor that alters the radiation reaction of the organism. Taking into consideration that the factors of hypokinesia induce a stress reaction, while stress depending on the phase of development increases or decreases the resistance of the organism to various stimulants and environmental factors, including radiation [5,6], one can conclude that the given modification of the radiation reaction is due to hypokinetic stress. With irradiation on the third day of hypokinesia (stage of mobilization of the general adaptation syndrome) the sensitivity of the animals to the ionizing radiations increases, which is manifest in early death, earlier and more significant weight loss of the body, spleen and testicles. Hypertrophy of the hypophysis and adrenal glands noted in the rats of the given group by the moment of irradiation indicates the incompleteness of the adaptive

reconstruction of the organism to the extreme hypokinesia. An increase in resistance to radiation in the group of animals irradiated on the 20th day of exposure to hypokinesia is linked to the formation in them at this period of increased nonspecific resistance. A similar effect was also obtained with the use of dosed electrical stimulation [7]. It was shown [8] that one of the mechanisms for increasing resistance under stress is migration of the lymphocytes from the lymphoid organs and the thymus to the bone marrow and activation by them of hemopoiesis. In the opinion of Koronakis and Sel'ye [9] in the process of evolution the organism has developed adaptive defense mechanisms against all types of stresses by creating passive tissue indifference or tolerance for a toxic agent (syntactical mechanism) and stimulation of reactions that accelerate the metabolic biotransformation of toxic substances (catatoxic mechanism). An important link in the mechanism of nonspecific resistance in a prolonged stress reaction is the period of systems functional changes into structural. The latter are persistently preserved even after the cessation of action of the stimulant, determining the future reactions of the organism to the external environmental factors [10]. Precisely the formation of structural traces in the process of hypokinetic stress can explain the preservation of increased resistance in rats to γ-irradiation in the period of restoration after 20-day hypokinesia.

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