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STATE OF THE BODY IN DISORDERS OF DIURNAL
PHYSIOLOGICAL RHYTHMS AND LONG-TERM HYPOKINESIA

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Translation of "Sostoyaniye organizma pri narushenii
sutochnykh fiziologicheskikh ritmov i dlitel'noy
gipokinezii," Vrachebnoye delo, No. 5, 1976, pp. 104-106

(NASA-TM-76051) STATE OF THE BODY IN
DISORDERS OF DIURNAL PHYSIOLOGICAL RHYTHMS
AND LONG-TERM HYPOKINESIA (National
Aeronautics and Space Administration) 7 p
HC A02/MF A01

880-22969

Unclas
CSCL 06S G5/52 46888



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

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STANDARD TITLE PAGE

NASA

1. Report No. TM-76051	2. Government Accession No.	3. Recipient's Catalog No.	
4. Title and Subtitle STATE OF THE BODY IN DIS- ORDERS OF DIURNAL PHYSIOLOGICAL RHYTHMS AND LONG-TERM HYPOKINESIA		5. Report Date March 1980	6. Performing Organization Code
		8. Performing Organization Report No.	
7. Author(s) S.N. Razin and A.V. Rychko Department of General Anatomy, Vinnitsa Medical Institute		10. Work Unit No.	
		11. Contract or Grant No. NASW-3199	
9. Performing Organization Name and Address Leo Kanner Associates Redwood City, CA 94063		13. Type of Report and Period Covered Translation	
		14. Sponsoring Agency Code	
12. Sponsoring Agency Name and Address National Aeronautics and Space Adminis- tration, Washington DC 20546			
15. Supplementary Notes Translation of "Sostoyaniye organizma pri narushenii sutochnykh fiziologicheskikh ritmov i dlitel'noy gipokinezii," Vrachebnoye delo, No. 5, 1976, pp. 104-106.			
16. Abstract In order to study the effects of hypokinesia and circadian rhythm restructuring on the morphological and functional status of the hypothalamo-hypophysio-adrenal system, young male Wistar rats were placed in small cages for varying periods. The animals were decapitated and preparations were made from sections of the brain and adrenals. Lipid deposition and atrophy were found in the adrenals and numerous destructive changes were noted in the investigated regions of the brain, indicating that the condition of these areas is directly affected by disruption of established rhythms in physiological processes.			
17. Key Words (Selected by Author(s))		18. Distribution Statement This copyrighted Soviet work is reproduced and sold by NTIS under license from VAAP, the Soviet copyright agency. No further copying is permitted without permission from VAAP.	
19. Security Classif. (of this report) Unclassified	20. Security Classif. (of this page) Unclassified	21. No. of Pages 7	22. Price

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STATE OF THE BODY IN DISORDERS OF DIURNAL
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Pathological changes in many of the body's functional systems may arise during frequent and long-term disruptions of the diurnal periodicity of basic physiological processes (A.N. Litsov, 1969, 1971; E. Buning, 1961).

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It has been established that prolonged restriction of motor activity is accompanied by morphofunctional changes in many organs and systems of the body. This involves disruptions of the structure of the musculoskeletal apparatus (V.V. Portugalov et al., 1971; G.A. Makarov, 1974; G.D. Rokhlin and E.P. Levitas, 1975), disorders of the cardiovascular system (M.G. Prives, 1971; B.S. Katkovsky and Yu.D. Pometov, 1971; O.M. Mikhaylova, 1974), organs of respiration and elimination (V.S. Baybara, 1971; I.S. Balakhovskiy et al., 1971), and disorders of the central and peripheral nervous systems (A.Ya. Tizul et al., 1972; A.A. Panov et al., 1973; V.V. Tkachev and E.N. Kul'kov, 1975).

The goal of this work was to study the morphofunctional rearrangement of the hypothalamo-hypophysio-adrenal system -- the primary hormone regulator of the body's involuntary functions -- during gross disruption of the rhythms in physiological processes in 12 hour (a day), protracted (30, 60, 90 days) restriction of motor activity. Taken into consideration were the reactions of the young, developing bodies of inbred animals to the influences we have discussed. Young (2.5 months) male Wistar rats were studied (exclusive of hormonal shift recurrence). Fifty animals were studied in all (8 -- the background group, and 7 animals each in experimental and control groups for each period of hypokinesia).

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The model for hypokinesia that we used was created by placing the animals in cages for from 7 to 19 hours, acutely restricting

*Numbers in the margin indicate pagination in the foreign text.

the animals' movements. Experimental animals were kept under usual vivarium conditions for the remaining time.

At the end of the experiment the rats were decapitated, body weight was determined, and the brain, hypophysis, and adrenals were removed. The latter were weighed on a torsion balance. All the data obtained were worked up using variation statistics.

The hypothalami and hypophyses were fixed in Bouin's fluid and the adrenals in 10% neutral formalin. Following removal the organs were covered in paraffin. Content of neurosecretory substances in the frontal sections (5-7 micrometers) of the hypothalamus in the supra-optic region, paraventricular nucleus, and hypothalamo-hypophyseal tract was determined using the Gomori-Gabou method, and the RNA was shown using Brasch's method. Hypophyseal preparations were stained using the Helm-Diban method, and the adrenals were stained with hematoxylin-eosin. In addition, sections from the adrenals obtained using a freezing microtome were stained with Sudan-III for the determination of lipids.

The obtained data indicate that the body's growth and development are arrested when physiological rhythms are grossly disturbed by artificial hypokinesia. Hence, the weight deficit of the experimental animals relative to the controls amounted to 28.1, 30.6, and 20% after 30, 60, and 90 days of hypokinesia, respectively.

Change in the adrenals was manifested by a sharp increase in the relative weight of the glands during the first period of motion restriction and decrease in these indices in the subsequent one. They did, however, remain at a higher level relative to the control group of animals (Fig. 1). Morphological changes in the adrenals after 30 days of the experiment were manifested by pronounced hypertrophy of the fascicular layer, and a large quantity of alveolar, vacuolized, and clear cells with spherical and pyknotic nuclei in them. A significant quantity of large drop lipids was observed in this layer, along with a decrease of them (relative to the controls) in the glomerular layer, and the appearance of lipid inclusions in the sudanophobic zone. Irregular borders between layers could be noted here and there. In the subsequent period of the experiment (60 and 90 days), atrophy of the adrenal cortices developed, borders between layers disappeared, and massive deposition

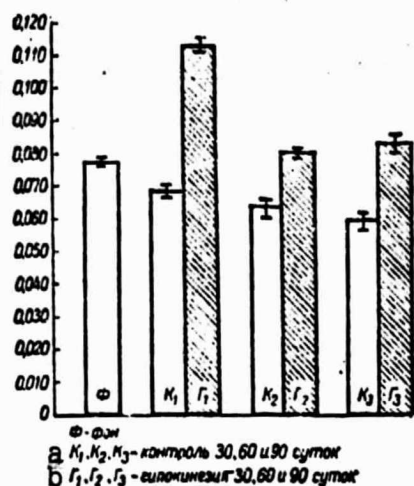


Fig. 1. Relative weight of adrenals in rats during hypokinesia.

Key: a. Control: 30, 60, and 90 days;
 b. Hypokinesia: 30, 60, and 90 days.

of large droplets of lipids was noted in the glomerular and fascicular zones.

Alterations in the paraventricular and supraoptic areas of the hypothalamus following 30 days of hypokinesia were characterized by acute dilation of the vascular network, a large quantity of dark cells, hypertrophied neurons with alveolar cytoplasm and degenerative pyknotic cells, which were sclerosed in places. Dilated axons filled with neurosecretory substance

were observed along the course of the hypothalamo-hypophyseal tract. The considerable accumulation of neurosecretory substance was present in the neurohypophysis around dilated sinusoidal capillaries. In the adenohypophysis there was a considerable decrease (relative to controls) of acidophilic cells and amphophils, and chromophobe secretions were noted.

These data are evidence that the hypothalamo-hypophyseal system is in a state of heightened functional activity, although degeneration of some structural elements and the appearance of heavy neurosecretion can already be distinctly observed. In the subsequent period of the experiment, the majority of the morphofunctional neurosecretory elements underwent irreversible destructive changes. The supraoptic region had a macrocellular neuroglial structure. There was an insignificant quantity of secretory neurons. They were of large size (acutely hypertrophied, with a considerable number of optically empty vacuoles, which filled the periphery of the neurons) and contained solitary large Gomori-positive granules, which were superficially adsorbed. A minor quantity of small neurosecretory granulations were discovered in the central paraventricular zone. Nissl bodies, in the form of small porous, pale lumps, were distributed between the vacuoles and accumulations of pyroninophilic

granulations in the central paraventricular zone. The remaining cellular structures of the nucleus were in various stages of regression. A part of the cells were determined to be pyknomorphic (stained only in places and having uneven contours). The other part was cell remnants -- membrane fragments. Their nuclei did not appear, and large vacuoles seriously deformed the contours of the cells. The capillaries were collapsed and neurosecretory substance did not appear in the dilated axons. In the base of the supraoptic area, where the hypothalamo-hypophyseal tract forms, small Gomori-positive granules were detected, and individual foci of large accumulations of neurosecretory substance were encountered here and there. Scanty content of small neurosecretory substance granules was noted around the vessels in the medial eminence. The posterior lobe of the hypophysis was degraded and had an alveolar structure. Solitary granules of neurosecretion were detected around the capillary dilatations of the main posterior part of the neurohypophysis. In its frontal lobe pronounced discomplexation of the trabeculae was noted, as was the predominance of chromophobes, the presence of colloid in the lumens of the gland's cells, and accumulation of it in the follicles of the intermediate lobe.

These data permit clarification of the dynamics of morpho-functional changes in the hypothalamo-hypophysio-adrenal system which bring about integration of its motor and involuntary functions. Self-regulation, through homeostatic reactions, is a property of the hypothalamo-hypophysio-adrenal system, as it is for any functional system. And since extramotor activity may not occur without corresponding shifts in metabolism and self-regulation, it is quite understandable that gross disruption of the rhythm of physiological processes, caused by hypokinesia, directly affects the condition of the cited systems (both in the central nervous system and in various forms of metabolism).

According to G. Sel'ye (1960), during a prolonged and intensive influence of stimulation, there first arises the reaction of "alarm," characterized by a sharp increase in the hormonal activity of the

adrenal cortex, after which there follows a growth in the body's resistance to the influence of both the given stress factor and of other factors qualitatively different from it. The exhaustion stage then arises, accompanied by a decrease in the body's resistance, which may lead to death. Morphofunctional changes in the hypothalamo-hypophysio-adrenal system following 30 days of hypokinesia are evidence that this system is in the resistance stage and is still capable of returning to its normal functioning state when the action of the stimulus is withdrawn and the normal rhythm of the body's physiological processes is restored. Later, following 60 and particularly 90 days of the experiment, a stage of pronounced exhaustion arose, characterized by irreversible changes in the hypothalamo-hypophysio-adrenal system.

Hence, the applied regime of 12 hours' hypokinesia during the most active period of the body's physiological rhythms has as pernicious an effect on the latter as the regime of more protracted daily maintenance of the animals in conditions of restricted motor activity. The young developing rat body is not capable of restructuring and adapting to a new rhythm of vital function. As a result, a stressful state develops, exhausting the defensive and adaptive potential of the body and capable of causing its death.

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