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EFFECT OF GRADED PHYSICAL LOAD ON THE STATE OF THE LIVER FROM MORPHOMETRIC DATA

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NATIONAL AERONAUTICS AND SPACE ADMINISTRATION WASHINGTON, D. C. 20546 FEBRUARY 1980 EFFECT OF GRADED PHYSICAL LOAD ON THE STATE OF THE LIVER FROM MORPHOMETRIC DATA AND BICCHEMICAL BLOOD INDICES OF RATS AGAINST A BACKGROUND OF HYPOKINESIA

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The research of recent years has given well deserved attention to the morpho- $/32^{**}$ functional condition of various organs and systems under the action of reduced mobility regimes [3,5,7-9]. Of particular interest in this connection is the liver, since its functional activity characterizes the condition of the organism. The effect of hypokinesia in depressing vital activity leaves no room for doubt, that hepatic changes appearing in this context fit into the framework of the hypokinetic syndrome [4,6]. We showed earlier [3], that there is genetic determination for a number of morphological and functional hepatic changes in 60-day hypokinesia. It is not known, whether these special features are maintained under conditions of rehabilitation following the hypokinetic syndrome. At the present time special attention should be given to developing concrete methods of prophylaxis and defense of the organism against the aftereffects of hypokinesia. For their elimination there are proposals for special types of physical training, for pharmacological intervention and for special gaseous media [1,2]. We felty that the solution to the problem referred to must not be limited to the discovery of auxiliary extraenvironmental experimental activities without taking into account the endogenic, genetically determined qualities of organic reactivity.

Method. The experiment was conducted on 100 sexually immature inbred male wats of the August and Wistar strains obtained from the "Stolbovaya" laboratory animal nursery of the Academy of Medical Sciences of the Soviet Union. Within the limits of the strains the animals were divided into 5 groups of 10 each. Group I served as controls and were kept in the ordinary accommodations of the vivarium. Group II were subjected to conditions of 60-day hypokinesia in small box cages we had special-

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ly constructed which restricted mobility during 23 hours, the animals spending the remaining hour in ordinary cages. Groups III, IV and V were kept under conditions of hypokinesia but in addition were subjected daily to rehabilitating physical loading on a treadmill. Training of group III rats began with 3 minutes on the treadmill with the belt traveling 30 m/min on day 1 of restricted mobility and was carried out each day. Every other day the length of the training period was increased by 1 minute and reached 30 minutes at the end of the experiment. The training of group IV was done in the same way except that the period was lengthened each day so that at the end it amounted to 60 minutes. Animals in group V were treated in the same way as those in group IV but daily, in addition to the physical load, they received IP phenamine (0.2 mg/100 g body wt). The experiment lasted 2 months and covered the period of most intensive growth to the time of sexual maturity. The animals were decapitated.

In the blood serum a determination was made of total protein using the biuret $\frac{33}{23}$ reaction, of total cholesterol using the method of Il'k, of beta-lipoproteins by the turbidimetric method, of aldolase activity using the method of V. I. Tovarnitski and Ye. I. Voluyskaya as modified by V. A. Anan'yev and V. R. Obukhova. In the blood a determination was made of the sugar content by the method of color reaction with orthotoluidine, in the liver glycogen content was determined by the antron method. The liver, taken from the abdominal cavity and prepared, was studied morphometrically by the method of V. A. Yermol'yev [3]. The data obtained were processed by the method of variation statistics on an "Iskra-12" electronic computer.

<u>Results and Evaluation.</u> An analysis of the results of morphometry (Table 1) testifies to the inhibiting effect of restricted mobility on the processes of hepatic growth in the rats of group II. In the rats of both strains we discovered a drop in the absolute mass of the liver. Under conditions of rehabilitating physical load (groups III and IV) and when such loading was combined with daily administration of phenamine (group V) one notes in all cases a positive correction for the aftereffects of restricted mobility for the liver mass. The mass's regeneration increases, as a rule, to a degree proportional with the increase in the rehabilitation load, i. e. from group III to group V. In this context rats of the August strain show a hepatic mass increase that does not change significantly from group II to group IV, whereas in group V, where the animals were also given phenamine, there is a sharp rise in the mass even to a point above the initial level.

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Against a background of intralinear differences conditioned by experimental effects one notes the appearance of authentic interlinear differences. In the Wistar rats there is a relatively uniform increase of hepatic mass from group II to group V. However, it should be remarked that under conditions of hypokinesia the Wistar animals seem to exhibit a higher threshold of resistance to the effect of mechanical loading. This explains the gradual growth of the hepatic mass in animals of the groups III, IV and V, in whose case work on the treadmill for 30 and 60 minutes and in the latter instance combined with pharmacological stimulation is far from being a threshold load, inasmuch as the liver mass of group V animals does not reach the level of the controls. The liver mass of group V August rats is slightly in excess of the control level; consequently 60 minutes physical loading in combination with phenamine appeared optimal. The mobility regimes of groups III and IV Wistar rats were far from threshold ones. In view of the animals' homogeneity in regard to sex, age and imposed load within the confines of the groups set up we are justified in explaining interlinear differences in terms of genotypical qualities of the rats of different pure breeds. The growth-inhibiting effect of restricted mobility is revealed likewise by an analysis of its linear dimensions (see Table 1). Rehabili-/34 tating physical loads obliterate and in some cases totally exclude the negative effects of the results of hypokinesia.

| | | | | | | | | | | | | EXPERIMENTAL |
|---|---------|-----|-----|--------|------|-------|------|--------|------|-------|-------|--------------|
|] | EFFECIS | AND | THE | STRAIN | 1 IC |) WHI | CH] | INBRED | RATS | BELON | WG (M | tm) |

| a | В Линия жи- | С Группа | | | | | | | |
|--------|--|--|---|---|--|--|--|--|--|
| | Пока атель вотных | 1+1 | 2-31 | 3+я | 4 - 51 | 3+2 | | | |
| d e | Абсолжтный Август вес. т Вистар Длина, си Август Вистар | $4,90\pm0,21$ $8,74\pm0,77^{\circ}$ $5,72\pm0,04$ $6,26\pm0,04^{\circ}$ | $4,25\pm0,13^{*}$ $5,13\pm0,09^{*}$ $4,86\pm0,06^{*}$ $5,3\pm0,04^{*}$ | 4,31±0,09* 5,63±0,10*° 5,47±0,09* 5,95±0,07* | 6,27±0,11** 5,20±0,06* 6,50±0,07** | 5,99=0,09* 6,72=0,05** | | | |
| f | Ширина, смА Август Вистар | 2.10 ± 0.03 2.27 ± 0.04 | 1,83±0,03* 1,97±0,04* | $2.39 \pm 0.05^{*}$ $1.92 \pm 0.05^{**}$ | 1,84±0,05* 2,03±0,03* | $1.59 \pm 0.02^{*}$ 2.03 ± 0.05^{-1} | | | |
| g | Толщина, смельтуст г Вистар | 0.95±0.04 0.76±0.03 | 0,75±0,02* 0,55±0,01** | 0,78.±0.03* 0,64=±0.62** | 0,76±0,02* 0,35=0,02** | $0.75 \pm 0.02^{\circ}$ $0.84 \pm 0.02^{\circ}$ | | | |

Remark. Here and in Table 2 asterisks show indices differing reliably from corresponding indices of rats in group I, circles show differences between the two strains.

Key: a. Index b. Strain

c. Group

- d. Absolute weight in g
- e. Length in cm
- f. Width in cm
- g. Girth in cm

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| | | Группа | | | | | | |
|---|---|---|---|--|---|--|--|--|
| · · · · · · · · · · · · · · · · · · · | Strain 1-1 | 2-11 | roup | l+1 | กรม | | | |
| Total protein in g% Aldolase, units | 6,33±0,06 7,10±0,08* 4,61±0,07 1,80±0,07 | 5,80 ⁻¹ .0,08* 6,30.1:0,10** 5,80*1:0,08* 6,20:1:0,09** | 6,85,1:0,10* 6,51 *=0,09** 6,41:1*0,08* 5,70 *=0,06* = | 9,48 + 0,09 + 6,10 + 0,10 + 4,23 + 0,05 + 3,79 + 0,07 + + | 6,55 + 0,06* 7,67 + 0,11** -1,63 + 0,10 -3,75 + 0,10 | | | |
| Hep.glycog.,mg% | E83,00 ±10,82 | 320,0:±5,41* 320,0 ±4,33* | 223,0±5,63* 250,0±2,16** | 207,0 1 3,25* 231,0 1 1,081 | 183.0 + 5,114 277.0 + 1,764 | | | |
| Blood sugar, mg% | 63,75 ± 1,30 67,00 ± 0,97 | 117,60:±0,86* 81,85*±1,19** | 90,07#10,97* 94,60.111,4** | 106,99 + 1,8+ | 82,11 + 0,2 64 68,03 + 1,19 | | | |
| Tot.cholest.,mg% | 85,0 ± 1,08 | 120,6:=0,97* 145,0:=1,52** | 111,6-1=1,84* 118,5-1=0,65** | 95.0 ± 0,96* 124,3±±1,4** | 78,0 ± 0,13* 106,0.5:1,84* | | | |
| 3-lipoprot., units | $3,18\pm0,22$ $3,20\pm0,22$ | 4,47:±0,09* 10,62±0,22** | 8,55±0,22* 7,53±0,10*° | 7,35==0,10+ 3,78==0,08*° | 6,02+=0,10* 8,74=0,09*° | | | |
| Key: A. Augus | t W | . Wistar | | | | | | |

TABLE 2. SOME BIOCHEMICAL INDICES IN CONNECTION WITH EXPERIMENTAL EFFECTS AND THE STRAIN TO WHICH INBRED RATS BELONG (M+m)

The results of biochemical studies (Table 2) under conditions of hypokinesia show a positive decrease in the indices for protein metabolism (total protein) and carbohydrate metabolism (hepatic glycogen); physical rehabilitation exercises and their combination obliterate the appearance of negative hypokinesia aftereffects or hinder them completely (total protein). This is not characteristic of the glycogen content; on the contrary, the level falls with the increase in load (exception: Wistar rats in group V). The tendency referred to can be explained, if we keep in mind that an increase in physical load is accompanied by an increase in glycogenolysis, as is shown by the sugar content in the blood. A definitely interesting point is the data on fat metabolism (cholesterol, beta-lipoproteins) and enzymatic metabolism (aldolase). Under conditions of 60-day hypokinesia the indices referred to certainly rise. In hypokinesia the organism accumulates a surplus of lipids due to its "functional inactivity" and hepatic functions are disrupted, as shown by the aldolase activity. Graded physical rehabilitation exercises favor the normalization of the changes that have appeared. It is a basic fact, that the interlinear differences established in the control for the biochemical indices under study are preserved no matter what the type of rehabilitating physical load. This speaks for the biological uniqueness of inbred rats of different pure breeds, which undoubtedly has a genotypic character.

Thus the present work has produced various types of confirmation for the effectiveness of proposed rehabilitation activities in preventing changes within the framework of the hypokinetic syndrome. The comparison of rats of different breeds within/35

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the limits of the experimental groups brought cut the hereditary nature of hepatic adaptation to physical loads and pharmacological intervention when there is restricted mobility.

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