RESTORATION OF STORED GLYCOGEN IN THE LIVER OF WHITE MICE FOLLOWING MUSCULAR STRESS WITH LIGATED PANCREATODUODENAL VEIN

M. F. Belovintseva and K. V. Savina

From the Laboratory of the Physiology of the Endocrine Glands (Head – Active Member of the AMN SSSR E. N. Speranskaya) I. P. Pavlov Institute of Physiology (Director – Academician K. M. Bykov) USSR Academy of Science, Leningrad.

(Received November 10, 1958. Presented by Academician K. M. Bykov)

It has been shown in E. N. Speranskaya's laboratory that insulin reduces liver function. After ligature of the pancreatoduodenal vein in dogs and rabbits, there was a change in the blood sugar curves during muscular work [2]; when the orifice of this vein was transferred from the portal to the inferior vena cava in dogs, a change in the rate of synthesis of new ethereal sulfate compounds was observed [3, 4]. In white mice, after ligature of the pancreatoduodenal vein, there was a reduction both in the glycogen content and in the cholinesterase activity of the liver [1]. The liver glycogen fell by 40% between the 4th and 16th days after the operation.

We required to find how glycogen loss caused by muscular work in animals with impaired liver function is made good. For this purpose, the following investigation was undertaken.

METHOD

Four sets of experiments were carried out on 127 white mice, and the glycogen liver reserves were determined under various experimental conditions. In the first group the liver glycogen content was determined in normal mice after muscular work, in the second group it was measured after ligature of the pancreatoduodenal vein, and in the third group the liver glycogen content in mice kept on a normal diet and with a ligature of the pancreatoduodenal vein was found; in the fourth group the same quantity was measured in mice with the ligature during muscular work after a 2-hour fast.

Ligature of the pancreatoduodenal vein was made under ether anesthesia. As a rule, the animals tolerated the operation well. In the II, III, and IV groups, animals were chosen in which the ligature had been applied 8 days previously. It is at this period that the most marked liver glycogen changes occur. A mock operation was carried out on the control animals. Both control and experimental animals were kept under the same feeding and living conditions. Before the experiment, they were starved for 2 hours; they were then killed by a swift decapitation, the liver was removed, dried on filter paper, and two portions weighed out on a torsion balance. Later these were treated with boiling alkali. Glycogen was determined by Simonovich's method [8], as modified by A. M. Genkin [5].

The results were analyzed statistically, because the variations in liver glycogen in mice are considerable. The figures treated included glycogen values varying from 0.3-3 g%; Experiment IV was an exception, and here very small amounts of glycogen were studied.

According to Stolzmann, Blawaska and Roth [10], the average liver glycogen content for white mice is 1.5-3.5 g%; the range of variation is very much greater, being from 0.3 to 3.5 g%. Muscular stress was caused by the animals swimming in water at 28° for 1 minute with a 2 g load attached to the tail.

Liver Glycogen Content in White Mice under Different Experimental Conditions

Number, in sequence	Date of experiments	Group I: liver glycogen (in g%) experiment mice	Group I: liver glycogen (in g%) control mice	Date of experiments	Group II: liver glycogen (in g%) experiment mice	Group II: liver glycogen (in g%) control mice	Date of experiments	Group III: liver glycogen (in g%) experimental mice	Group III: liver glycogen (in g%) control mice	Date of experiment	Group IV: liver glycogen (in g%) experimental mice	Group IV: liver glycogen (in g%) control mice
1	2/10/1958	0,49	1,71	11/11/1957	1,83	1,28	2/21/1958	0,42	1,93	4/1/1958	0,24	0,28
2	2/10/1958	1,01	1,85	11/11/1957	1,84	2,46	2/21/1958	0,63	2,87	" " "	0,26	0,34
3	2/10/1958	0,92	2,21	11/11/1957	1,20	2,68	" " "	0,61	1,97	" " "	0,21	0,37
4	2/13/1958	1,64	0,53	11/14/ "	0,66	1,88	" " "	0,32	1,95	" " "	0,22	0,87
5	2/13/1958	2,39	0,51	11/14/ "	0,49	1,88	" " "	1,11	1,77	" " "	0,28	0,39
6	2/13/1958	1,50	2,38	11/14/ "	0,91	1,38	" " "	0,67	1,14	" " "	0,25	1,85
7	2/14/1958	1,73	1,95	11/14/ "	0,76	1,22	3/24/1958	1,02	1,85	4/4/1958	0,14	1,85
8	2/14/1958	1,30	2,47	" " "	1,74	2,44	" " "	0,72	1,28	4/4/1958	0,14	0,51
9	2/14/1958	1,35	1,87	3/18/ "	0,50	1,98	3/28/1958	0,87	1,36	" " "	0,82	0,61
10	2/16/1958	0,90	1,29	3/18/ "	0,77	1,23	" " "	0,88	0,89	" " "	0,26	
11	2/27/1958	2,51	0,60	" " "	1,57	1,45	" " "	1,92	2,58	" " "	0,1	Average 0,73 g% ±0,15
12	2/27/1958	1,00	0,59	" " "	2,20	1,57	" " "	1,86	2,65	" " "	0,1	
13	2/27/1958	0,75	1,10	" " "	0,52	1,22					0,16	
14	2/27/1958	0,60	0,51	" " "	1,44	1,85		Average 0,86 g% ±0,26	Average 1,85 g% ±0,10			
15	2/28/1958	0,80	1,90	" " "	0,32						Average 0,24 g% ±0,03	
16	2/28/1958	0,44	2,57	" " "	0,50	Average 1,85 g% ± 0,30						
17	2/28/1958	0,38	0,72	" " "	1,93							
18	2/28/1958	0,44	0,64	" " "	1,62							
19	2/28/1958	2,50	0,54		Average 1,15 g% ± 0,24							
20	3/2/ 1958	1,48	1,19									
21	3/3/ 1958	1,95	1,11									
22	3/3/ 1958	0,33	1,06									
23	3/3/ 1958	0,40	1,68									
24	3/3/ 1958	0,76										
25	3/11/1958	0,98	Average 1,31 g% ± 0,20									
26	3/11/1958	0,37										
		Average 1,11 g% ± 0,10										

RESULTS

In Group 1, 49 experiments were carried out, 26 with muscular work, and 23 without (controls). The results showed that the glycogen content of the control group was 1.31 g%, and that of the experimental group 1.11 g% (see Table). Thus the moderate amount of muscular work entailed by swimming for one minute with a 2g load causes a 15% fall in liver glycogen. Their results agree with published figures [7, 10 and others].

In group II, 32 experiments were performed, 18 on mice with a ligature of the pancreatoduodenal vein, and 14 on controls. The results are given in the table. It can be seen that the average liver glycogen value in the control mice was 1.85 g%, and in the experimental group 1.15 g%, i.e. the operation reduced liver glycogen by 0.7 g% or 38%; this agrees completely with results which we obtained previously [1]. Thus, breaking the path by which insulin reaches the liver causes a greater reduction in glycogen (38%) than does moderate muscular exercise (15%).

In Group III, 24 experiments were carried out, and of these 12 were performed on animals with a ligatured pancreatoduodenal vein, and 12 on controls. Both groups were exercised by swimming. The animals were then kept for 2 hours under normal conditions and with normal feeding. It was found that after swimming, the liver of the experimental group contained 0.86 g% of glycogen, while the value for the control group was 1.85 g%.

In comparing results of the experiments in Group II and Group III, it can be seen that muscular work in animals with reduced liver function causes a glycogen deficit which is not made good in 2 hours, while in the control group a 2-hour normal feeding period is sufficient for a complete restoration of the original glycogen level in the liver.

In Group IV, 22 animals were used, and of these 13 were used for the experiment and 9 served as controls. As previously, the animals swam while loaded, after which they were starved for 2 hours until they were killed and the liver samples taken.

It is known that fasting causes a considerable liver glycogen loss [6, 9 and others]. As the experiments on Group IV showed, in the operated group, after muscular work and a 2-hour fast, the glycogen reduction was considerable, while in the control group it was less. After exercise, the average amount of glycogen in the liver of the operated animals was 0.24 g%, and in the controls 9.73 g%. It may be concluded that alteration of the usual route along which insulin passes to the liver not only reduces the amount of glycogen stored in the liver but also interferes with the building up of further supplies, thus indicating an impaired hepatic function.

SUMMARY

Alterations were made to the route by which insulin entered the liver, and stored glycogen investigated.

Ligature of the pancreatoduodenal vein caused a reduction of 38% in the amount of glycogen stored.

It was shown that moderate muscular exercise in operated animals causes a glycogen expenditure which is not fully compensated by the normal diet.

LITERATURE CITED

[1] M. F. Belovintseva, Probl. endokrinol. i gormonoter., No. 2, pp. 3-6 (1957).

[2] M. F. Belovintseva, Probl. endokrinol. i gormonoter., No. 2, pp. 35-40 (1957).

[3] M. F. Belovintseva, Theses and Reports at the Conference on Problems of the Role of Neurohumoral and Hormonal Factors in Nervous Activity in Health and Disease,* Leningrad, 1956, p.12.

[4] M. F. Belovintseva, E. N. Speranskaya, in book: Radiobiology.* Moscow, 1958, pp.251-257.

[5] A. M. Genkin, Biokhimiya, No. 4, pp.546-555 (1938).

[6] N. O. Kon'kov, The Effect of Different Conditions on the Amount of Liver Glycogen.* Dissertation. St. Petersburg, 1876.

* In Russian.

[7] L. G. Leshkevich, Changes in the Amount of Glycogen in Muscles, Liver, Heart, and Brain, and the Level of Sugar and of Lactic Acid in the Blood During Prolonged Muscular Exercise.* Leningrad, 1956.

[8] S. Simonovits, Bioch. Ztschr. 265, 347-439 (1933).

[9] P. H. Herbert, R. H. Mole. J. Endocrinol., 1956, v.14, p.188-196.

[10] Stolzmann, Blawaska and Roth, Bull. Soc. amins. sc. et. lettr. (Poznan, 1956), N. 6.

*In Russian.