BIOCHEMISTRY AND BIOPHYSICS

THE ROLE OF THE NERVOUS SYSTEM IN THE REGULATION OF TISSUE RIBOFLAVIN CONTENT

E.V. Danetskaya

From the Section of Physiology and Nutritional Hygiene (Chief-Prof. B. I. Kadykov) of the Leningrad Scientific Research Sanitary Hygienic Institute (Director-Corresponding Member AN SSSR Prof. N. F. Galanin)

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It is well established that animals having a diet inadequate in riboflavin develop a serious illness, ariboflavinosis, which is characterized along with other symptoms by the development of trophic disturbances and retardation of regenerative processes.

The trophic ulcers that develop in the course of ariboflavinosis resemble in some respects those trophic ulcers so resistant to therapy that arise after the intactness of individual nerves has been disturbed. This circumstance led us to the thought that there may be an association between riboflavin levels in the organism and the trophic function of the nervous system.

To clarify this question three series of experiments were performed in the course of which we studied the role played by the nervous system in the accumulation of riboflavin in the tissues of the animal organism.

EXPERIMENTAL METHODS

The experiments were done on white rats weighing 150-200 g. The animals were maintained on a full synthetic diet with supplementation of the essential vitamins.

In choosing the organ to be denervated we decided on the liver as being richest in riboflavin and therefore the most suitable.

Our first series of experiments was performed on 45 white rats with denervated livers.

Following the operation within 2, 4, 10, 20, 30, 60 and 70 days the animals were sacrificed in groups of 5 to 8 and the riboflavin content of their organs (liver, kidneys, heart, striated muscles) was determined.

Tissue riboflavin determinations were made by the S.E. Kaplan method.

This procedure is based on extraction of riboflavin from the organs by means of methyl alcohol and determination of the degree of fluorescence under ultraviolet rays.

EXPERIMENTAL RESULTS

Fig. 1 presents the riboflavin content of various organs of rats that had their livers denervated and the tissues removed for study at the different times after the operation.

As can be seen from the figure, the amount of riboflavin present drops sharply as soon as the 2nd day following liver denervation this taking place within liver tissue itself (by 49%) as well as in other organs (in kidneys by 37%, in heart by 50%).

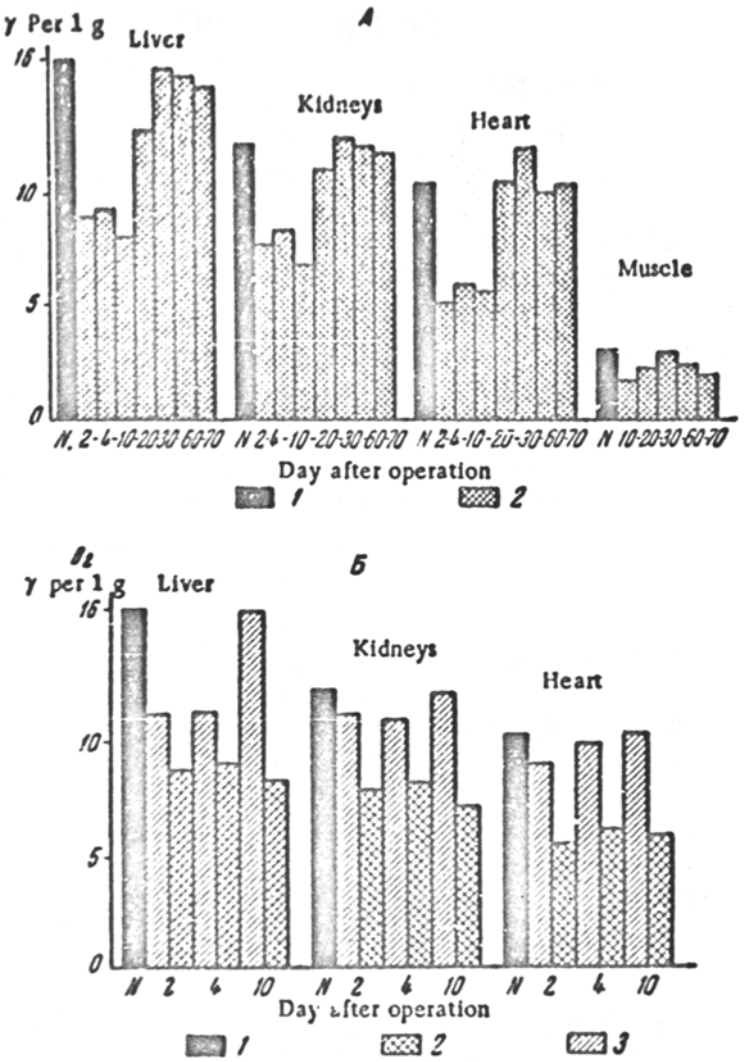

Fig. 1. Riboflavin content of rat organs at various time intervals after the operation denervating their livers.
1) normal; 2) after denervation; 3) control trauma. A, B) different experimental series.

The riboflavin level continued depressed even on the 4th and 10th days after the operation. By the 20th day the riboflavin would rise in the liver as well as the other organs reaching normal levels only by the 30th post-operative day.

It may be supposed that by that time there developed a certain degree of compensation for the disturbed nervous connections although the mechanism of such an adjustment remains unexplained.

It must be pointed out that the liver denervation performed by us was incomplete as we did not disturb the fibers accompanying the blood vessel net.

After we had performed the experiments with the denervated livers, we felt a need to determine whether the alterations in the tissue riboflavin levels were due to nerve fiber destruction only or whether they were a post-traumatic effect.

To clarify the point a second experimental series was run.

Twenty-five animals of this group were maintained under conditions similar to those in the first group

and were then subjected to procedures undergone by the animals of the first series with the sole exception that their livers were not denervated.

At various time intervals after their operations, these rats were sacrificed and the riboflavin content of their organs then determined.

The influence that traumatization of the liver has upon riboflavin content in the organs of white rats is shown in Fig.1, 3.

As can be seen from the Figure, operational trauma leads to some depression of the riboflavin content of the liver but this is much less than when accompanied by denervation. The amount of riboflavin within the liver in these experiments returned to normal as soon as the 10th day, i.e., much more rapidly than after denervation. The level of riboflavin in the other organs remained almost unaffected.

It follows, therefore, that the riboflavin depression obtained in the first series of experiments occurs in the organs and tissues of the rats as a result of liver denervation and that the nervous system of the liver, when intact, must participate in some basic manner in the riboflavin metabolism of the organism.

In order to clarify the role played by the liver in the riboflavin alterations within the organs and tissues which occur after the liver had been denervated, a third series of experiments was performed.

In twenty-five animals of this group, 0.5 cm of the right sciatic nerve was resected. At various times after this operation, the rats were sacrificed and the riboflavin content of their organs was determined.

The quantity of riboflavin present in the rat tissues after the sciatic nerve had been sectioned is represented in the table.

Riboflavin Present in Rat Organs After Resection (0.5 cm) of the Right Sciatic Nerve (in μg)

Riboflavin content in μg	Normal rats				After operation											
					4th day							10th day		69th day		75th day
								Calf muscle								
	Liver	Kidney	Heart	Calf muscle	Liver	Kidneys	Heart	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Minimum	13.6	10.4	8.4	1.8	14.8	12.4	10.0	0.2	2.8	0	2.2	0.2	2.2	0	2.8		
Maximum	19.6	12.5	12.1	3.4	16.4	14.6	10.4	0.3	2.4	0.4	3.4	0.4	3.6	0.4	3.8		
Average	16.0	12.3	10.4	2.3	15.5	13.2	10.1	0.25	2.6	0.2	2.8	0.3	2.6	0.2	2.8		

As is evident from this table, the amount of riboflavin present in the liver, kidneys and the heart was the same after resection of the sciatic nerve as before the operation. Only in the right calf muscle was there a sharp diminution in the riboflavin content after the right sciatic nerve had been resected, this decrease never becoming compensated.

The amount of riboflavin present in the left calf muscle (with undisturbed innervation) was 2.2-3.8 μg per 1 g, this corresponding to the riboflavin present in the muscles of normal rats.

This evidence indicates that irreversible destruction of a nerve leading to a muscle causing the nerve to degenerate provokes a constant diminution in the amount of riboflavin in the calf muscle while in the other muscles and organs such alterations do not take place.

In this manner there was established the basic difference between disturbing the intact innervation of the liver and sectioning the sciatic nerve in so far as these maneuvers affect the riboflavin content of the tissues. Severing the sciatic nerve depressed only the quantity of riboflavin present in the denervated muscle tissue, not affecting the content of this vitamin in other organs and tissues, while denervation of the liver altered the amount of riboflavin present not only in the liver but also in other organs.

This leads to the conclusion that the nervous system participates not only directly in the regulation of the riboflavin contents of tissues but also indirectly through its effect on the liver which, when denervated in our experiments, resulted in prolonged depression of the riboflavin content in other organs and tissues.

SUMMARY

The nervous system has two ways in which it affects the riboflavin level within the organism. It does so directly as in the experiment in which severing the portion of the sciatic nerve leading to a calf muscle depressed the riboflavin content of that muscle almost to the vanishing point. It does so indirectly as in the experiment in which denervation of the liver decreased the riboflavin content in kidneys, heart and striated muscles.

LITERATURE CITED

S.E. Kaplan, The Influence of Dietary Albumin Upon the Riboflavin Requirements of the Organism* Dissertation, Moscow, 1947.

* In Russian.