OXYGEN CONSUMPTION BY THE BRAIN AND ITS GLYCOLYTIC ACTIVITY AFTER THE INTRODUCTION OF VARIOUS DOSES OF SEROTONIN INTO THE ORGANISM

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In a series of investigations to determine the role of the central nervous system in the mechanism of the action of insulin, we studied the influence of various doses of serotonin upon the sugar level in the blood and the development of the nervous syndrome during hyperinsulinism [1]. In this case we proceeded on the basis of the information of a number of authors [5, 6], that serotonin reduces the glucose consumption and absorption of oxygen by the brain. It was assumed that if the development of nervous symptoms after the injection of insulin is due to hypoxia [2, 3], then insulinization against a background of exogenous injection of serotonin may lead to more severe disturbances of the function of the central nervous system and thereby serve as an indication of the participation of the brain in the mechanism of the action of insulin. However, the results of our investigations did not confirm this hypothesis. It was found that small doses of serotonin (2 mg/kg) do not influence the blood glucose level, while when the preparation is injected in doses of 5 mg/kg, the blood sugar concentration is increased for two hours. The injection of various doses of serotonin against a background of well developed insulin hypoglycemia does not influence the intensity of the manifestation of the nervous symptom complex in comparison with the control.

The need arose for a more detailed study of the influence of serotonin upon the metabolism of individual organs, in particular, the brain. As tests for characterizing the influence of serotonin upon the central nervous system, we selected the level of absorption of oxygen and the glycolytic activity, since the intensities of these processes in the brain determine its functional state and the participation of this organ in various nervous manifestations under the influence of various pharmacological and hormonal preparations.

EXPERIMENTAL PROCEDURE

The experiments were conducted on white rats of both sexes, weighing 180-200 g. The animals were kept on a normal diet. Serotonin was injected in physiological saline intramuscularly in doses of 2.5, 5, 7.5, 15, 25, and 50 mg per kg of weight of the animal. Two hours after the injection of the preparation, the rats were decapitated, the brain removed, and the oxygen consumption and glycolytic activity determined in slices. The absorption of oxygen by the brain tissue was studied by a manometric method in a Warburg apparatus in Krebs-Ringer-phosphate buffer (pH 7.3) at 37° for an hour. The glycolytic activity was measured according to the level of lactic acid, determined according to Barker and Summerson [4] during incubation of the brain tissue in a glucose-salt solution (pH 7.3) for an hour at 37°.

Among the control animals we studied the oxygen consumption and glycolytic activity of the brain without the injection of serotonin. Moreover, in experiments in vitro we determined the influence of serotonin, introduced into the incubation medium, upon the absorption of oxygen and the intensity of glycolysis of the brain tissue.

TABLE 1. Oxygen Consumption by the Rat Brain under the Influence of Various Doses of Serotonin (M ± m)

No. of animals	Injection of serotonin (in mg/kg)	Oxygen consumption (in microliters per 100 mg crude tissue per h)	P
5	Norm (healthy animals)	117±3	
6	2,5	118±8	>0,1
6	5,0	120±5	>0,1
6	7,5	113±8	>0,1
5	15,0	116±4	>0,1
5	25,0	113±3	>0,1
8	50,0	114±6	>0,1

TABLE 2. Glycolytic Activity of Rat Brain Tissue after Intramuscular Injection of Various Doses of Serotonin* (M ± m)

	Amount of lactic acid (in micromoles/g)						
	control	two hours after injection of serotonin (in mg/kg)					
		2,5	5	7,5	15	25	50
Preformed lactic acid	2,9±0,11	2,4±0,09	2,3±0,11	2,3±0,12	2,8±0,08	2,7±0,10	2,7±0,07
P		<0,001	<0,002	<0,002	>0,1	>0,05	>0,05
Increase in an hour of incubation	9,2±0,45	7,5±0,36	7,5±0,23	7,6±0,77	9,2±0,29	8,9±0,41	9,0±0,44
P		<0,01	<0,01	<0,05	>0,1	>0,1	>0,1

*Each series of experiments was conducted on five animals.

TABLE 3. Glycolytic Activity of Rat Brain Tissue after Introduction of Serotonin* (M ± m)

Conditions of expt.	Amount of lactic acid (in micromoles/g)	
	preformed	increase in an hour of incubation
Control	2,6±0,08	9,1±0,34
Introduction of 0,5 mg serotonin per 100 mg of tissue	2,6±0,11	6,9±0,31
P	>0,10	<0,001

*The experiments were conducted with brain tissue of 10 animals of each series.

EXPERIMENTAL RESULTS

After the introduction of small doses of serotonin (2.5-7.5 mg/kg), the respiration slowed down in individual animals after 45-60 min. Under the action of higher doses (15-50 mg/kg), after 30-45 min, all the animals exhibited adynamia, pronounced cyanosis of the limbs and brain, bradypnoea, involuntary urination, and other symptoms characterizing a disturbance of the function of the central nervous system.

The results of an investigation of the influence of various doses of serotonin upon the oxygen consumption and glycolytic activity of the brain tissue, as well as the data of the control experiments, are presented in Tables 1, 2, and 3.

As can be seen from Table 1, when various doses of serotonin are injected (from 2.5 to 50 mg/kg), the oxygen consumption by the brain is unchanged. Fluctuations in the level of absorption of oxygen in comparison with the control data are statistically unreliable. Thus, the results of our experiments do not confirm the investigations of certain authors, who indicate that serotonin reduces the absorption of oxygen by brain tissue. Moreover, serotonin

added to the incubation medium in experiments in vitro appreciably inhibits the oxygen consumption by brain tissue, which is 122 ±4 microliters per 100 g of crude tissue in the control experiments, and 108 ±4 in the experiments with addition of serotonin ($P < 0.05$).

On the basis of the data cited, we should have assumed that serotonin, when introduced into the animal organism, would be broken down under the influence of aminooxidase, and therefore would not influence the intensity of the absorption of oxygen by the brain. However, the data on the influence of serotonin upon the glycolytic activity of the brain tissue under identical experimental conditions, contradict this hypothesis. Thus, when serotonin is administered in doses of 2.5, 5, and 7.5 mg/kg, the glycolytic intensity is substantially reduced, while doses of 15, 25, and 50 mg/kg have no effect upon the glycolytic activity (see Table 2). In experiments in vitro, we also succeeded in establishing that serotonin in a dose of 0.5 mg per 100 mg of crude weight of tissue causes a statistically reliable decrease in glycolysis (Table 3).

In these experiments it is paradoxical that the high doses of serotonin, when injected into the organism, do not influence the glycolytic intensity, while smaller amounts of this preparation inhibit the activity of glycolytic processes. The mechanism of this phenomenon is obscure.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of the first issue of this year.
