HEXOKINASE ACTIVITY OF HOMOGENATES OF BRAIN AND CARDIAC AND STRIATED MUSCLE OF NARCOTIZED ANIMALS

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Diminished utilization of glucose by the tissues has been reported during narcosis [1-6]. Not enough is known about the state of enzyme systems concerned with glycolysis under such conditions.

In the present paper we present data relating to the activity of the glucokinase reaction in brain, heart, and striated muscle tissues of narcotized rats.

EXPERIMENTAL METHODS

Hexokinase activity was assessed in tissue homogenates by Long's method [7], with the difference that tissue proteins were precipitated by cadmium hydroxide, instead of by zinc hydroxide. The results are expressed as milligrams/1 g of tissue/h. As a result of glycogenolysis taking place during incubation this value may be lowered. Special experiments performed with tissues of normal and narcotized rats showed, however, that increase in glucose content either did not take place, or it was insignificant. In only 3 out of 32 experiments was there any appreciable rise in glucose content (by a maximum of 3 to 10 mg/1 g of tissue/h). Reducing sugar was determined in blood taken immediately after terminating narcosis. In experiments involving profound ether narcosis we also determined the reducing sugar content of protein-free homogenates of tissue homogenates.

For the measurement of hexokinase activity of myocardial and brain tissues we performed 4 series of experiments. In the first, control series, the animals were not anesthetized. The animals of the second series were subjected to deep ether narcosis, of short duration. Inhalation of ether was uninterrupted for 15-30 min, and was stopped when respiration became slow, or was arrested. In this group, blood sugar was found to be 27% above that of the control series, and in heart muscle and brain 11 and 5% above the control values, respectively. In the third series, the rats were maintained under light ether narcosis for 90-120 min (ether administered for 3-5 min at 2-5 min intervals). Unconsciousness was continuous in this group, breathing was regular, and the corneal reflex was not abolished; blood sugar remained within normal limits. The animals of the fourth series were rendered unconcious by subcutaneous injection of 1.5-2 ml of 4% pentothal. Unconsciousness lasted for 54-60 min, during which time their breathing was regular, and their blood sugar within normal limits.

EXPERIMENTAL RESULTS

According to Long and to other workers, the hexokinase activity of normal rats varies within wide limits. We found that the same applied to narcotized rats.

The figures given in Table 1 represent the mean values obtained for each series of experiments. In the three series of narcotized rats the mean levels of hexokinase activity of heart muscle were raised above that of controls by 28, 50, and 28%, respectively; appreciable rise in brain hexokinase activity (32%) was found in the animals of the group subjected to prolonged light narcosis. The wide variations in hexokinase activity of the tissues are such that this result cannot be considered as being statistically significant.

Striated muscle has a relatively low hexokinase activity, and a high glycogen content. For these reasons, we adopted a different experimental procedure for the examination of this tissue. The hexokinase activity of striated muscle of single animals was determined at the beginning and the end of the period of narcotization. Groups of adductor muscles of the left and right hind legs were used for this purpose (Table 2).

TABLE 1. Glucokinase Activity* of Myocardial and Brain Tissues of Narcotized Rats

Tissue examined	Control			Ether narcosis								Pentothal narcosis, duration 45-60 min			
				profound, duration 15-30 min				light, duration 90-120 min							
	number of experiments	limits of variation	arithmetic means	no. of experiments	limits of variation	arithmetic means	percentage change (of mean values)	no. of experiments	limits of variation	arithmetic means	percentage change (of mean values)	no. of experiments	limits of variation	arithmetic means	percentage change (of mean values)
Heart	16	7—28	14	12	2—45	18	+28	14	8—35	21	+50	5	7—24	18	+28
Brain	14	11—36	22	12	15—40	23	+4	15	18—58	29	+32	5	6—36	23	+4

*Glucokinase activity is expressed as fall in glucose content in milligrams of 1 g of tissue in 1 h.

TABLE 2. Glucokinase Activity of Striated Muscle at the Beginning and End of Ether Narcosis

No. of experiment	Duration of narcosis	Glucokinase activity (mg/g/h)		Change
		beginning of narcosis	end of narcosis	
1	30	2,4	4,8	+2,4
2	30	1,0	6,4	+5,4
3	30	10,9	5,2	—5,7
4	90	2,4	3,4	+1,0
5	90	4,7	3,7	—1,0
6	90	13,5	11,2	—2,3
7	120	5,4	2,4	—3,0
8	120	15,0	18,0	+3,0
9	120	1,6	3,2	+1,6
10	120	3,2	1,4	—1,8
11	120	4,7	13,2	+8,5
Mean		5,9	6,6	

It is evident from the data of this table that narcosis had no significant effect on the glucokinase activity of striated muscle.

Our experiments have thus given no indication of any fall in glucokinase activity of brain, myocardium, or striated muscle of rats under ether or pentothal narcosis. In some cases, an increase in glucokinase activity was observed in heart muscle. A rise in the glucose content of the blood and tissues of animals under deep ether narcosis suggests that utilization of glucose by the tissues of anesthetized animals is lower than in controls; this finding is in full agreement with numerous published reports. The fall in utilization of glucose by the tissues cannot in this case be related to lowering of glucokinase activity, but must be due to some other factors.

It is conceivable that, because of changes in its hormonal regulation, the permeability of cells of narcotized animals to glucose may be lowered, thus hindering formation of the substrate-enzyme complex.

This hypothesis needs further investigation for its establishment.

SUMMARY

The hexokinase activity of homogenates of myocardial and brain tissues of rats, as assessed by Long's method, was not lowered by profound ether narcosis of short duration (15-30 min), or by light, prolonged (90-120 min) ether anesthesia; there was a tendency towards increased activity in the heart muscle. It is concluded that the reduced carbohydrate metabolism of anesthetized animal tissues cannot be due to interference with its initial step, viz., the glucokinase reaction.

It is suggested that depression of carbohydrate metabolism of anesthetized animals may be due to diminished permeability of the cells to glucose.

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