Injection of actinomycin D 1 h before swimming prevented the appearance of both peaks of enzyme activity, evidence of its synthesis *de novo* (Table 2). To study the possible role of the lysosomal apparatus in induction of G6PDH synthesis, vinblastine or colchicine was injected in a series of experiments into the rats 1 h before swimming. The G6PDH activity of these animals fell by 15-18% relative to the control after swimming and remained at this level at all subsequent times of observation. A similar effect was produced by gordox, an inhibitor of lysosomal proteolytic activity. The inhibitors used in this investigation had no action on G6PDH in experiments *in vitro*.

It can thus be concluded from these results that intensive physical exercise leads to induction of synthesis of G6PDH, the key enzyme of the pentose phosphate pathway, in the rat liver. Initiation of this synthesis is preceded by activation of lysosomes and there translocation toward the nucleus. The effect of blockers of lysosomal translocation and of the inhibitor of proteolytic activity confirms the writers' hypothesis that lysosomes participate in the mechanism of induction of enzyme protein synthesis *de novo*. Since the actinomycin block abolishes the inducing effect of lysosomes, lysosomal enzymes most probably intervene at the transcription level.

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SEROTONIN CONTENT IN DIFFERENT PARTS OF THE BRAIN, LIVER, INTESTINE, AND BLOOD OF RATS PREDISPOSED AND NOT PREDISPOSED TO ALCOHOL CONSUMPTION

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The contradictory nature of results obtaine during the study of the effect of ethanol on the serotoninergic system during exposure to the acute and chronic action of alcohol, and pharmacologic analysis of the role of this system in the regulation of voluntary alcohol consumption have not provided an unequivocal answer to the question of its role in the mechanisms of alcohol motivation [9]. The possiblity of preliminary selection of animals (noninbred albino rats) predisposed and not predisposed to alcohol consumption, on the basis of the duration of alcohol narcosis [3], discovered previously, makes it possible to study the

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TABLE 1. Effect of Ethanol (2.5 g/kg, intraperitoneally) on Serotonin Content in Parts of Brain, Liver, Intestine (in μg/g) and Blood (in μg/ml) in Rats Predisposed and Not Predisposed to Alcohol Consumption

Test object	Rats predisposed to alcohol consumption		Rats not predisposed to alcohol consumption	
	control	ethanol	control	ethanol
Hypothalamus	1,58±0,07***	1,23±0,03***	1,00±0,017	1,498±0,125**
Thalamus	0,86±0,04**	1,08±0,015***	1,012±0,025	0,84±0,03***
Brain stem	0,53±0,008***	0,65±0,02***	0,43±0,01	0,632±0,036***
Corpus striatum	0,47±0,01***	0,314±0,02***	0,59±0,088	0,41±0,018***
Liver	0,51±0,01***	0,71±0,09***	0,62±0,007	0,74±0,02***
Intestine	0,67±0,01***	0,61±0,02	0,53±0,01	0,66±0,03**
Blood	0,115±0,004***	0,222±0,004***	0,159±0,007	0,237±0,003***

Legend. Differences between two control groups and between control group and action of ethanol significant at the **P < 0.01 and ***P < 0.001 levels; five animals used in each group in the experiments.

initial characteristics of various systems of a metabolic [3], neurochemical [5, 6], hormonal [2], and behavioral nature [6, 1] in these animals.

The aim of the present investigation was to study the serotonin content in various parts of the brain and at the periphery during administration of ethanol of rats predisposed and not predisposed to alcohol consumption.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male albino rats weighing 200-300 g. The animals were divided, depending on the duration of alcohol narcosis (dose of ethanol 4.5 g/kg, injected intraperitoneally as a 25% solution) into predisposed (duration of side position 62 ± 18 min) and not predisposed (196 ± 23 min) to alcohol consumption. The content of serotonin in the hypothalamus, thalamus, brain stem, corpus striatum, and also in the intestine, liver, and blood was determined in the animals 2 weeks after testing. The corresponding parameters also were determined 30 min after intraperitoneal injection of ethanol into the animals in a dose of 2.5 g/kg. The animals were put to sleep with ether before tissues were taken for investigation. Serotonin was determined spectrofluorometrically [9] on an Opton (West Germany) spectrofluorometer. Statistical analysis of the data was carried out by Student's test [7].

EXPERIMENTAL RESULTS

The experiments showed (Table 1) that the serotonin level in animals predisposed to alcohol consumption was higher in the hypothalamus and brain stem and lower in the thalamus and corpus striatum. Considering these results and the opposite relations discovered previously between the duration in the side position after injection of ethanol and predisposition to alcohol consumption [3], it can be postulated that the initially high level of alcohol motivation was connected with the character of serotonin distribution in the various parts of the brain: an increased concentration in the hypothalamus and brain stem and a reduced concentration in the thalamus and striatum. The potentially low level of alcohol motivation corresponded to opposite relationships in the serotonin content in the brain structures mentioned above.

Typological differences in the serotonin content in noninbred rats predisposed and not predisposed to alcohol consumption also were reflected in differences in the peripheral component of the serotoninergic system: the serotonin concentration in animals
period of alcohol narcosis was higher in the intestine and lower in the liver and blood.

Under the influence of ethanol, on the whole changes in rats of both groups in the peripheral component of the serotoninergic system were in the same direction: The serotonin concentration in the liver and blood was increased (Table 1). The serotonin level in the intestine of animals predisposed to alcohol consumption, in which it was reduced somewhat by ethanol, was an exception. These facts may indicate accumulation of serotonin at the periphery under the influence of alcohol; in rats predisposed to alcohol consumption, moreover, increased liberation of this biogenic amine could take place from the intestine, the main source of peripheral serotonin [8].

In rats of both groups changes in the serotonin concentration following exposure to a single dose of ethanol also were in the same direction in the corpus striatum (decrease) and in the brain stems (increase), indicating that these changes in the structures mentioned are

nonspecific in character. Conversely, changes in the serotonin concentration in the hypothalamus and thalamus were in opposite directions in animals predisposed to alcohol consumption (lowered in the hypothalamus, raised in the thalamus) and in animals not predisposed (raised in the hypothalamus, lowered in the thalamus). Under these conditions, the changes in the relationships between the serotonin concentration caused by ethanol can be regarded from the standpoint of a specific connection between these changes and the attitude of the animals toward alcohol consumption, which was positive in the first case and negative in the second.

With respect to the mechanisms of alcohol motivation, the most important discovery was the differences found in the principal motivation zone, i.e., the hypothalamus. Clear correlation was established previously between the ability of ethanol to active structures of positive reinforcement (facilitation of self-stimulation) and the onset of a liking for it in rats [4]. Considering data in the literature on the presence of an autonomous system of serotoninergic neurons, inhibiting self-stimulation [11], in the hypothalamus it can be postulated that in animals predisposed to alcohol consumption, with a high serotonin concentration in the hypothalamus, from the beginning the influence of this system on the structures of positive reinforcement is more powerful. Under the influence of ethanol these inhibitory influences are evidently weakened (this is shown, perhaps, by the decrease in the serotonin concentration in the hypothalamus found under these conditions) and, consequently, the systems of positive reinforcement are activated and a "positive" emotional state develops. In animals not predisposed to alcohol consumption, the positive reinforcement system is probably less inhibited from the state by influences from the serotoninergic system of the hypothalamus (the serotonin concentration in this region is lower). Under the influence of ethanol the inhibitory influences mentioned above evidently increase in these animals and, consequently, under the conditions under discussion a positive emotional state cannot arise.

The results described above thus suggest a possible modulating role of the serotoninergic system of the hypothalamus in the positive or negative effects of ethanol in noninbred albino rats predisposed and not predisposed to alcohol consuption.

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