20. K. Lukowiak and W. F. Colmers, "Endogenous peptides work at multiple sites in the nervous system in the control of gill behavior in Aplysia," *Regul. Pept.*, **17**, 99–109 (1987).
21. H. R. Olpe and V. Baltzer, "Vasopressin activates noradrenergic neurones in the rat Locus coeruleus: a microiontophoretic investigation," *European J. Pharmacol.*, **73**, 377–378 (1981).
22. T. Onaka, M. Hamamura, and K. Yagi, "Suppression of vasopressin secretion by classically conditioned stimuli rats," *Japan J. Physiol.*, **36**, No. 6, 1261–1266 (1986).
23. L. P. Renaud and A. Padjen, "Electrophysiological analysis of peptide actions in neural tissue," in: *Centrally Acting Peptides*, MacMillan Co., New York (1978), pp.59–84.
24. S. J. Sara, J. Barnett, and P. Toussant, "Vasopressin accelerates appetitive discrimination learning and impairs its reversal," *Behav. Proc.*, No. 7, 159 (1982).
25. T. B. G. Van Wimersma, J. M. Van Ree, and D. H. G. Versteeg, "Neurohypophyseal peptides and avoidance behavior: the involvement of vasopressin and oxytocin in memory processes," in: *Neuropeptides and Neural Transmission*, C. A. Marsan and W. Z. Traczyk (eds.), Raven Press, New York (1980), pp. 293–300.

CHANGE IN THE BLOOD GLUCOSE LEVEL UNDER THE INFLUENCE OF "FAILURE" OF AN AVOIDANCE REACTION

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The testing of nootropic preparations has proven most effective in the presence of stress-induced functional disturbances of higher nervous activity [1, 3, 4]. Thus, the positive effect of nootropic agents increases sharply in the presence of stress brought about by "failure" of a developed avoidance reaction (AR), even if it was not manifested before the "failure" [1].

In view of the great significance of the stress factor for the testing of psychotropic preparations, the determination of the stress level with respect to any physiological parameter is highly desirable, for example, with respect to the blood glucose concentration, which increases in the presence of stress. One of the methods which permits the determination of the blood glucose level is based on the utilization of biochemical reactions unfoding on a solid carrier, the Multistix multilayered color film [5].

The aim of the present study was the investigation of the blood glucose concentration in the presence of a "failure" of an avoidance reaction.

The experiments were carried on 19 mongrel male rats, weighing 180–200 g. An AR was developed in a shuttle chamber in 12 of these over the course of five days (25 presentations each daily). The conditional stimulus (a sound of 800 Hz) was present 10 sec in isolation, following which the electric current was turned on. The running of the animal into the other half of the chamber turned off both stimuli. The intersignal period ranged from 30–60 sec. The "failure" of the developed AR was achieved by the unforeseen change of the relationships between the conditional stimulus and the current, on the one hand, and between the reaction and the current, on the other. The running of the animal in response to the conditional or unconditional stimuli did not lead to their switching off during three runs, so that the animal received the shock. The current was switched off immediately after the third reaction, and the sound 2 sec later. The experiment was then carried on according to the previous protocol (20 presentations).

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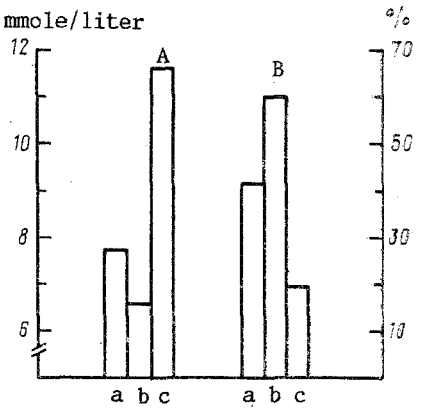

Fig. 1. Change in AR after "failure" in rats with low (A) and with high (B) blood glucose level. a) Glucose level, mmole/liter; b, c) respectively, number of rats (%), the conditioned reflex activity of which deteriorated or improved.

TABLE 1. Blood Glucose Concentration in Rats of Different Groups

Parameters	Groups			
	first	second		third
		before "failure"	after "failure"	
Avoidance reactions, %	—	78,1±7,6	68,0±8,2*	88,0±5,8
Glucose concentration, mM	3,6±0,4	5,8±0,4	8,5±0,4	8,9±0,3**
n	7	6		6

Notes. *) $p < 0.05$ relative to the average before "failure"; **) $p < 0.01$ relative to the first group.

The animals were divided into three groups on the basis of the conditions of the measurement of glucose: the first, an intact control from the vivarium; the second, animals in which the blood glucose concentration was determined twice, before and after the disruption of the RA which was accomplished the following day after additional experience with the development of the RA; the third, animals in which the blood glucose concentration was determined only after the "failure" of the RA. A drop of blood was taken from the tail of each rat and placed on the surface of the Multistix so as to cover the entire reactive surface; after 30 sec the drop was blotted with filter paper. The intensity of the color was determined by comparison with a standard scale graded in mmole/liter. The results were analyzed on an Amstrad (England) personal computer using the Kolmogorov–Smirnov test.

The experimental data show that the blood glucose concentration increases as the degree of the stressing of the animals, in accordance with the conditions of the experiment, by the development and the "failure" of the RA (Table 1). In particular, the glucose level increases following "failure" which elicits a reliable decrease in the RA; this confirms the hypothesis regarding the increase in the animals' state of stress as a result of this procedure [1].

We should note that the glucose level following the effect in the second group of rats in which the measurement was made twice (before and after the "failure") did not differ significantly from that in the third group with a one-time measurement only after the "failure". It can be hypothesized on the basis of the data obtained that repeat measurement under the conditions indicated above does not lead to a substantial additional increase in this parameter. This permits its measurement before and after the "failure" in the same animals, which economizes on the number of animals and the amount of work involved.

Since the glucose concentration did not differ significantly after the "failure" in the rats of the second group and the third groups, they were combined in order to establish the character of the change in the RA as a function of the glucose level, and accordingly of the level of stress induced by the change in the condition of the experiment, in a larger sample. This sample was then divided into two new groups: group A, which included animals with a blood glucose level after the "failure" less than 8.5 mmole/liter, and group B, which included animals with a concentration after the "failure" equal to or exceeding 8.5 mmole/liter.

It was found that the number of RA before the "failure" in group B was greater than in group A, i. e., a higher blood glucose concentration, i. e., a higher level of sequelae of stress, corresponds to higher RA values before "failure." It was also shown that in the rats of group A, with a lower blood glucose level, and accordingly with a lesser state of stress, the number of RA after the disruption of the experimental procedure mainly increased, and, contrariwise, in the presence of a greater state of stress the number of RA decreased after the "failure" in the main group of animals (Fig. 1). The above is in agreement with previously obtained data [2].

Thus the RA "failure" procedure employed in these experiments leads to stressing of the rats, which is reflected in an increase in blood glucose concentration. The number of RA after the "failure" mainly increases in rats with a lower blood glucose concentration, and correspondingly with a lesser state of stress, and, contrariwise, the number of RA mainly decreases where there is a higher glucose concentration and greater stress.

LITERATURE CITED

1. A. N. Inozemtsev and L. L. Pragina, "Reversible disruption of the avoidance reaction as an experimental model for the study of the action of psychotropic preparations on higher nervous activity," *Zhurn. Vyssh. Nervn. Deyat.*, **39**, No. 4, 764–766 (1989).
2. A. N. Inozemtsev and F. F. Kokaeva, "The features of functional reversible 'failure' of the avoidance reaction in rats," *Zhurn. Vyssh. Nervn. Deyat.*, **40**, No. 2, 386–388 (1990).
3. L. L. Pragina, A. N. Inozemtsev, V. V. Ashapkin, et al., "The influence of some psychotropic preparations on the coditioned reflex memory of rats," in: *The Comparative Physiology of Higher Nervous Activity of Man and Animals*, Vol. 1 [in Russian], (1988), p. 173.
4. A. Cavoy, A. Ennaceur, and J. Delacour, "Effects of piracetam on learned helplessness in rats," *Physiol. and Behavior*, **42**, No. 6, 545–549 (1988).
5. H. Wisser, "Klinisch-chemische analytic mit mehrschiehtfilmtechnic," *Fresenius J. Anal. Chem.*, **342**, No. 3–4, 242–243 (1986).