carcinogens thus cause functional desympathization of organs and tissues, and they may thereby create the conditions for disturbance of regulation of normal metabolism of the cells and their subsequent malignant transformation under the influence of carcinogens and their metabolites in the tissues themselves.

LITERATURE CITED

1. V. K. Gurkalo, Éksp. Onkol., No. 1, 24 (1983).
2. V. K. Gurkalo, M. A. Zabezhinskii, G. B. Pliss, et al., Byull. Éksp. Biol. Med., No. 4, 455 (1977).
3. R. K. Kavetskii, Interaction between Host and Tumor [in Russian], Kiev (1977).
4. K. P. Balitskii (ed.), Mechanisms of Antitumor Resistance [in Russian], Kiev (1978).
5. G. B. Pliss, Vopr. Onkol., No. 3, 95 (1978).
6. A. V. Syromyatnikov, Éksp. Onkol., No. 2, 38 (1980).
7. A. V. Syromyatnikov, Éksp. Onkol., No. 3, 10 (1983).
8. V. Ya. Fel' (editor), Cytologic Aspects of the Primary Action of Chemical Carcinogens [in Russian], Leningrad (1982).
9. V. S. Sheveleva, Ontogenetic Formation of Neurohumoral Regulation of Excitation in Host Tissues and Carcinogenesis [in Russian], Leningrad (1974).
10. E. C. Miller and J. A. Miller, Cancer (Philadelphia), 47, 1055 (1981).
11. P. Stein-Werblowsky, Exp. Neurol., 42, 97 (1974).

EFFECT OF ETHIMIZOLE* ON INSTRUMENTAL LEARNING IN RATS

G. Yu. Borisova

UDC 615.214.31.015.4:612.821.1/.3

KEY WORDS: ethimizole; learning; conditioned reflex.

The beneficial effect of ethimizole on short-term and long-term memory and the more rapid formation of natural and artificial functional connections have been observed in several investigations [1, 3, 4, 10]. However, data on the effect of ethimizole on learning, when different types and schemes were used, are contradictory. For instance, conditioned reflex formation in mice and rats was impaired by the use of large doses (5-10 mg/kg) of ethimizole [2]. Formation of conditioned defensive and blinking reflexes in rabbits was delayed in some experiments [8] by ethimizole (1-2 mg/kg). In dogs ethimizole (1-3 mg/kg) disturbed differentiation [9]. However, ethimizole had a positive action on the formation of an active avoidance reflex to painful electrical stimulation in rats trained in a Y-maze [6] and also improved learning of a spatial alternation of food reinforcement reflex in a complex maze [12]. Ethimizole also had a beneficial effect on the formation of long-term and short-term verbal memory and on learning and consolidation in man [5].

Considering the contradictory nature of information on the character of the effect of ethimizole on learning in man and animals, it was decided to study the action of this drug on the formation of conditioned reflexes of varied complexity, and with reinforcement of different modalities.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male rats weighing 180-200 g. The techniques used differed in the complexity of the response to be formed and the modality of reinforcement. A conditioned active avoidance

*1-Ethylimidazole-4,5-dicarboxylic acid-bis-methylamide.

Department of Pharmacology of Memory and Behavior, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad.

(Presented by Academician of the Academy of Medical Sciences of the USSR N. P. Bekhtereva.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 6, pp. 705-706, June, 1985. Original article submitted October 22, 1984.

TABLE 1. Effect of Ethimizole on Instrumental Learning in Rats

Method	Interval between injection of drug and beginning of training, h	Percent of CAAR on last day of training		Number of combinations required to reach criterion	
		control	ethimizole (3 mg/kg)	control	ethimizole (3 mg/kg)
Y-maze with food reinforcement	0,5	—	—	108,0±15,1	135,0±20,9*
Y-maze with nociceptive reinforcement	0,5	27	7*	—	—
	3,0	35	15*	—	—
Shuttle box	1,0	46	54	—	—
	3,0	48	56	—	—
Shuttle box (single dose)	3,0	29	31	—	—

Legend. *P < 0.05.

reflex (CAAR) was formed in an automated shuttle box by the method described previously [11] and in a Y-maze. The conditioned stimulus was light, and for nociceptive reinforcement electric shocks were used (voltage 1.5 times the threshold of pain sensation). The rats were trained for 5 days (20 tests daily). Visual differentiation with food reinforcement was formed in the same maze. Pieces of cheese (0.20-0.25 g) were used as reinforcement. Differentiation was formed in the course of 2-6 days to the level of 90% of correct responses (eating cheese in the illuminated arms of the maze). The number of combinations of conditioned and unconditioned stimuli required to reach the criterion was counted. Ethimizole (3 mg/kg) was injected subcutaneously or intraperitoneally daily, 30 min and 1 or 3 h before learning. The animals of the control group received physiological saline.

EXPERIMENTAL RESULTS

A single injection of ethimizole in a dose of 3 mg/kg given 30 min before learning did not change the number of CAAR in the shuttle box compared with the control [1]. Daily administration of ethimizole to the rats 30 min before training in a Y-maze disturbed formation of the reflex with nociceptive and food reinforcements (Table 1). The effect of ethimizole was thus independent of the character of reinforcement. Considering that 1 h after a single injection of ethimizole an increase in the rate of RNA synthesis is observed [7], the rats were trained in the shuttle box and in the Y-maze having previously received ethimizole 1 and 3 h before learning. During CAAR formation in the shuttle box the number of correct responses by rats trained after receiving ethimizole was the same as in the control, but differentiation with nociceptive reinforcement proved more difficult to form in the Y-maze (Table 1).

To rule out any disparity between the biochemical effects of a single injection of ethimizole on RNA synthesis and the duration of learning in the present experiments (up to 6 days), CAAR were formed in a shuttle box in the course of one session (50 combinations) and ethimizole was injected 3 h before training. However, in this case also no positive effect of ethimizole on learning was found.

Regardless of the time of injection of the drug and the modality of reinforcement, no improvement of learning was thus observed in these experiments under the influence of ethimizole. However, analysis of CAAR formation in a shuttle box after administration of ethimizole, when training was temporarily interrupted, showed that the deficit of skill, usually observed in the control [1], was absent. It can accordingly be postulated that ethimizole, by stimulating RNA synthesis within a definite time interval, promotes consolidation, i.e., an optimal level of RNA synthesis is evidently needed for fixation of an acquired skill. The positive effect of ethimizole on the consolidation stage also is supported by the longer preservation of acquired skills in rats receiving a single dose of ethimizole, after the completion of training [11].

Consequently, the positive effect of ethimizole on memory is connected, not with improvement of learning, but with its action on the consolidation stage, and the use of a single dose of this drug after the end of training may be considered to be worth while.

LITERATURE CITED

1. G. Yu. Borisova, Abstracts Lodged with the All-Union Institute of Scientific and Technical Information, No. 5242-80 (1980).
2. Yu. S. Borodkin, in: Pharmacology of New Sedatives and Their Clinical Uses [in Russian], Leningrad (1962), p. 156.

3. Yu. S. Borodkin and V. A. Krauz, Pharmacology of Short-Term Memory [in Russian], Moscow (1978).
4. Yu. S. Borodkin and Yu. V. Zaitsev, Neurochemical and Functional Bases of Long-Term Memory [in Russian], Leningrad (1982).
5. Yu. V. Zaitsev and S. S. Losev, Fiziol. Cheloveka, No. 1, 175 (1979).
6. Yu. V. Zaitsev and N. S. Sapronov, in: Neurotransmitters and the Mechanism of Action of Neurotropic and Cardiovascular Drugs [in Russian], Moscow (1979), pp. 24-25.
7. O. G. Kulikova, L. M. Belyavtseva, and N. I. Razumovskaya, in: Abstracts of Proceedings of the 9th All-Union Conference on Biochemistry of the Nervous System [in Russian], Erevan (1983), p. 290.
8. L. A. Samoilova and V. S. Sabanov, in: Neuropharmacology (New Preparations in Neurology) [in Russian], Leningrad (1980), p. 152.
9. A. T. Selivanova, T. E. Kolosova, N. N. Lazuko, et al., in: Neuropharmacology (New Preparations in Neurology) [in Russian], Leningrad (1980), p. 154.
10. V. M. Smirnov and Yu. S. Borodkin, Artificial Stable Functional Connections [in Russian], Leningrad (1979).
11. N. V. Khromov-Borisov, G. Yu. Borisova, I. Ya. Aleksandrova, et al., Zh. Vyssh. Nerv. Deyat., No. 4, 761 (1978).
12. P. D. Shabanov and S. Yu. Kalishevich, in: Abstracts of Proceedings of the 3rd Congress of Pharmacists of the Lithuanian SSR [in Russian], Vilnius (1982), p. 112.

CONTRACTILITY OF ISOLATED AORTIC STRIPS FROM RATS WITH STABLE ARTERIAL HYPERTENSION DUE TO LONG-TERM ADMINISTRATION OF CEREBROSIDES

S. A. Mirzoyan, O. P. Sotskii, É. S. Sekoyan, A. V. Topchyan, and G. M. Sarkisova

UDC 616.12-008.331.1:547.952

KEY WORDS: cerebrosides; arterial hypertension; vascular smooth-muscle cells; calcium channels.

There is growing factual evidence that neurochemical mechanisms participate in the regulation of the cerebral circulation [1, 2]. Further research in this direction has shown that glycosphingolipids (GSL), one of the neurochemical components of the brain, have a marked action on cerebral vessels [3] and reveal the cell-membrane mechanisms of their vasocontrictor effect [4]. These findings, and also data showing a raised blood GSL level in cerebrovascular pathology [5, 7] and arterial hypertension [11], and the ability of cerebrosides, under experimental conditions, to induce stable arterial hypertension [12], determined the aim of the present investigation, which was to study contractility of smooth-muscle cells (SMC) of strips of the abdominal aorta of rats during long-term administration of cerebrosides to the animals.

EXPERIMENTAL METHOD

Experiments were carried out on nonbred male albino rats weighing 140-160 g. The total cerebroside fraction was isolated from bovine brain [13] and then purified on a column with mark L silica-gel (Chemapol, Czechoslovakia). Cerebrosides in a dose of 5 mg/kg, in the form of a suspension made up in a mixture of ethanol and physiological saline (1:20), were injected intraperitoneally (0.5 ml) daily for 4 months. Animals of the control group received the same volume of the ethanol–physiological saline mixture. The blood pressure (BP) was measured by a noninvasive physiological saline mixture. The blood pressure (BP) was measured by a noninvasive

Department of Pharmacology and Department of Bioinorganic and Biophysical Chemistry, Erevan Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 6, pp. 706-708, June, 1985. Original article submitted August 17, 1984.

 0007-4888/85/9906-0762$09.50