BRAIN LEVELS OF SOME MEDIATORS IN RATS WITH NEUROGENIC GASTRIC LESIONS

I. S. Zavodskaya, V. V. Bul'on, and E. V. Moreva

UDC 612.822.2.015.3:577.175.82]-08

KEY WORDS: hyperstimulation; neurogenic lesions of the stomach; mediators.

Research in the Department of Pharmacology of the Research Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, has shown that the center for reflexes concerned in the development of neurogenic lesions of internal organs is located in the hypothalamus [1]. A previous pharmacologic analysis by the writers showed that adrenergic and cholinergic central synapses participate in the transmission of impulses causing the development of visceral lesions [4]. This is confirmed also by the results of biochemical investigations, in which hyperstimulation of animals was accompanied by a sharp fall in concentrations of acetylcholine and noradrenalin in the tissues of the hypothalamus [4]. Electron-microscopic studies showed that during hyperstimulation of animals leading to damage to the tissues of the internal organs, definite disturbances of the intracellular structure of the hypothalamic supraoptic nucleus develop. There was a marked decrease in size of the active zones in the synaptic terminals, together with destruction of vesicles containing acetylcholine and noradrenalin [3].

The object of this investigation was to study the role of other neurotransmitter systems in the central mechanism of transmission of impulses disturbing trophic processes in the gastric mucosa during hyperstimulation. For this purpose, the concentrations of dopamine, histamine, serotonin, and GABA in brain tissue were determined.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male albino rats weighing 180-200 g, obtained from the "Rappolovo" Nursery, Academy of Medical Sciences of the USSR. Before the experiment, the animals were deprived of food for 2 days. Neurogenic lesions of the stomach were induced in two ways [1]. The first way was immobilization with simultaneous electrical stimulation for 3 h through needle electrodes inserted into muscle of the forelimbs. Electrical stimulation was by square ac pulses generated by an ÉST-12 electronic stimulator with a frequency of 50 Hz, pulse duration 10 msec, output voltage 8-10 V (on 10 immobilized rats). The second way was by mechanical stimulation of the pyloroduodenal reflexogenic zone, caused by application of Pean's forceps for 10 min. The animals were killed 3 h after trauma. Visual observation of the stomachs showed that both types of stimulation caused a well-defined lesion of the mucosa: hyperemia, edema, ulceration. The animals were decapitated, the brain was quickly removed, the cerebellum and cortex were discarded, leaving the brain stem, including di- and mesencephalon and medulla, for investigation. Concentrations of dopamine, histamine, and serotonin were determined fluorometrically [5, 6, 15] and GABA by electrophoresis on paper [12]. Intact animals served as the control.

EXPERIMENTAL RESULTS

The dopamine content in the brain region chosen for investigation did not change significantly either during electrical stimulation of immobilized rats for 3 h or during reflex stimulation of the pyloroduodenal region (Table 1).

Hyperstimulation, leading to neurogenic lesions of the stomach, was accompanied by a change in the histamine and serotonin concentrations in brain tissue. For instance, elec-

Laboratory of Experimental Pharmacology, Department of Pharmacology, Research Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 97, No. 2, pp. 135-136, February, 1984. Original article submitted July 15, 1983.

0007-4888/84/9702-0147$08.50

TABLE 1. Concentrations of Some Mediators (in μg/g) in Brain Tissue of Control Rats and Rats with Neurogenic Lesions of the Stomach (M ± m)

Mediator	Immobilization + electrical stimulation for 3 h		Trauma to pyloroduodenal region	
	Control	Experiment	Control	Experiment
Dopamine	1,9±0,03 (5)	2,1±0,07 (5)	1,6±0,04 (10)	1,8±0,05 (9)
Histamine	1,1±0,06 (10)	0,88±0,04* (9)	1,4±0,04 (7)	0,95±0,07** (7)
Serotonin	0,70±0,04 (15)	0,56±0,02* (15)	0,70±0,03 (8)	0,50±0,03** (7)
GABA	368±30 (15)	260±20* (15)	—	—

Legend. Number of experiments shown in parentheses. *P < 0.005; **P < 0.001.

trical stimulation of the rats for 3 h led to a decrease in histamine concentration from 1.1 ± 0.06 to 0.88 ± 0.04 μg/g wet weight of tissue, i.e., by 20% compared with normal. After trauma to the duodenum, there was an even greater fall in the histamine concentration in the brain region studied: by 30% compared with the initial level.

Similar changes also were observed in the serotonin level. In animals with neurogenic lesions of the stomach caused by electrical stimulation for 3 h the brain serotonin concentration fell from 0.70 ± 0.04 to 0.56 ± 0.02 μg/g, and after application of forceps to the pyloroduodenal region it fell from 0.70 ± 0.03 to 0.50 ± 0.30 μg/g.

Besides a change in the histamine and serotonin balance in the brain tissue of the experimental animals changes also were observed in the level of GABA which, in the modern view, is an inhibitory mediator in certain brain structures. Its concentration after electrical stimulation for 3 h was 30% lower than in the control.

The results now obtained showing changes in the mediator levels in the rat brain during hyperstimulation, leading to the development of neurogenic lesions of the stomach, are in agreement with the observations of other workers who studied biogenic amine and GABA metabolism in the brain during exposure to various kinds of stress [2, 7, 11, 13, 14].

Changes in concentration of mediators (noradrenalin, acetylcholine, histamine, serotonin, and GABA), observed by the writers previously and also in the present experiments, were accompanied by a disturbance of energy and structural metabolism in the CNS. For instance, during hyperstimulation leading to neurogenic lesions in the internal organs, the concentrations of glycogen, creatine phosphate, and cyclic AMP in the brain tissue fall, accompanied by considerable changes in the genetic apparatus of nerve tissue cells [8-10].

During hyperstimulation of animals, causing lesions of the stomach, besides a fall in the concentrations of the principal CNS mediators (acetylcholine and noradrenalin), the concentrations of histamine, serotonin, and GABA also decrease. It can be tentatively suggested that not only are cholinergic and adrenergic nerve structures involved in the central mechanism of development of neurogenic gastric lesions, but histaminergic, serotoninergic, and GABA-ergic systems also are concerned.

LITERATURE CITED

1. S. V. Anichkov, I. S. Zavodskaya, E. V. Moreva, et al., Neurogenic Dystrophies and their Pharmacotherapy [in Russian], Leningrad (1969).
2. Ya. I. Azhipa, Nerves of Glands of Internal Secretion and Mediators in the Regulation of Endocrine Functions [in Russian], Moscow (1976), pp. 288-290.
3. I. S. Zavodskaya and R. P. Kucherenko, Dokl. Akad. Nauk SSSR, No. 3, 732 (1971).
4. I. S. Zavodskaya and E. V. Moreva, Pharmacologic Analysis of the Mechanism of Stress and Its Sequelae [in Russian], Moscow (1981).
5. E. B. Laboda and A. Yu. Makarov, Lab. Delo, No. 4, 219 (1974).
6. É. Sh. Matlina and T. B. Rakhmanova, in: Methods of Investigation of Some Systems of Humoral Regulation [in Russian], Moscow (1967), pp. 136-141.

7. F. Z. Meerson, Adaptation, Stress, and Prophylaxis [in Russian], Moscow (1981), pp. 200-215.
8. É. A. Migas, Byull. Éksp. Biol. Med., No. 5, 541 (1976).
9. É. A. Migas and T. N. Nilova, Byull. Éksp. Biol. Med., No. 9, 316 (1980).
10. E. V. Moreva and V. V. Bul'on, Farmakol. Toksikol., No. 6, 625 (1979).
11. V. S. Raitses, T. N. Semenyuk, and L. I. Aftanas, in: Stress and Adaptation [in Russian], Kishinev (1978), pp. 191-192.
12. N. R. Shatunov and A. I. Sytinskii, in: The Nervous System [in Russian], Vol. 3, Leningrad (1962), pp. 12-16.
13. L. Eroglu and S. Atamer-Simsek, Arzneimit.-Forsch., 30, 2115 (1980).
14. B. J. Hirschowitz, Annu. Rev. Pharmacol., 19, 203 (1979).
15. P. A. Shore, A. Burkhalter, and V. Cohn, J. Pharmacol. Exp. Ther., 127, 182 (1959).

EFFECT OF HYPOXIC AND HYPERCAPNIC ATMOSPHERE AND LOW AMBIENT TEMPERATURE ON FUNCTION OF THE HYPOTHALAMUS—PITUITARY—THYROID SYSTEM IN RATS

S. S. Mogutov, A. M. Zaichik, and E. S. Sergeeva

UDC 612.826.4+612.432+612.441].014.464

KEY WORDS: ambient atmospheric factors; temperature; hypothalamus—pituitary—thyroid system; physiological state.

Exceptionally close attention is currently being paid to the creation of conditions modifying reactivity of warm-blooded animals. The physiologically most adequate conditions, similar to those leading to the development of natural hypobiosis, are those attainable through the combined use of an altered atmosphere and low ambient temperature. It has been shown that these factors can be used to obtain deep hypothermia [12, 14], to create a stable state of depressed vital activity and of artificial hypobiosis [11], and to develop increased resistance of the organism to the action of stress stimuli of various kinds by measured cooling of rats once or twice under conditions of increasing hypoxia and hypercapnia [3]. However, the pathophysiological mechanisms of interaction between organism and altered atmosphere have not yet been adequately studied. In particular, despite the importance attached to the hypothalamus—pituitary—thyroid system in the formation of resistance [1, 6, 9, 15], there are no data on the characteristics of response of this division of the neuroendocrine system of animals during cooling under conditions of hypoxia and hypercapnia.

This paper describes a study of the dynamics of hypothalamus—pituitary—thyroid function of rats during cooling in a modified atmosphere.

EXPERIMENTAL METHOD

Experiments were carried out on 239 noninbred male rats weighing 180-200 g. The experiments were carried out in the fall and winter at the same time of day. The animals were cooled to a rectal temperature of 20.4 ± 0.03°C by the method of Giaja and Andjus [12, 14]. The O_2 and CO_2 concentrations in the pressure chamber and the rectal temperature of the rats were measured before and after exposure. Material (hypothalamus) for histologic study was taken after decapitation of the animals 20, 50, 70, 90, and 120 min after the beginning of exposure and 48 h after its end. Blood was taken at the 20th, 70th, and 120th minutes of cooling and 3 h after cooling. To assess the state of thyroid and pituitary function the

Central Research Laboratory and Department of Pathologic Physiology, Leningrad Pediatric Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR B. A. Lapin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 97, No. 2, pp. 136-139, February, 1984. Original article submitted March 5, 1983.

0007-4888/84/9702-0149$08.50