LITERATURE CITED

1. I. P. Anokhina and G. D. Zabrodin, in: Stress and Its Pathogenetic Mechanisms [in Russian], Kishinev (1973), pp. 11-13.
2. E. A. Gromova, in: Memory and Trace Processes (Abstracts of Proceedings of the Second Conference on Problems in Memory and Trace Processes) [in Russian], Pushchino-on-Oka (1970), p. 46.
3. E. A. Gromova, in: Memory and Trace Processes (Abstracts of Proceedings of the Third Conference on Problems in Memory and Trace Processes) [in Russian], Pushchino-on-Oka (1974), p. 111.
4. E. A. Gromova, N. A. Zemtsova, M. B. Zykov, et al., in: Stress and Its Pathogenetic Mechanisms [in Russian], Kishinev (1973), p. 62.
5. É. Sh. Matlina, A. M. Baru, and V. N. Vasil'ev, in: Progress in Science and Technology. Series: "Physiology of Man and Animals," Vol. 15, Physiology of Emotions [in Russian], Moscow (1975), p. 30.
6. N. B. Essman, in: Biology of Memory (Symposium), Budapest (1971), pp. 213-238.
7. E. A. Gromova, in: Second International Congress of CIANS, Abstract, Prague (1975), p. 135.
8. T. P. Semyonova (T. P. Semenova), in: Second International Congress of CIANS, Abstract, Prague (1975), p. 72.
9. B. Welch and A. Welch, Anal. Biochem., 30, 161 (1969).

EFFECT OF COPPER, MANGANESE, AND COBALT IONS ON CHEMICAL SENSITIVITY OF INTEROCEPTORS

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The effect of copper, manganese, and cobalt on the chemical sensitivity of interoceptors was studied in acute experiments on 82 cats. Injection of cuprous chloride was found to cause reversal of blood pressure and respiratory reflexes to acetylcholine, cobaltous chloride weakened these reflexes, whereas manganous chloride potentiated them. The changes observed in the interoceptive reflexes are considered to depend mainly on the direct action of the trace elements on interoceptor function.

KEY WORDS: *Trace elements; acetylcholine; blood pressure; reflex reactions.*

The role of trace elements in the physiological activity of man and animals is now firmly established [1-3]. However, the role of trace elements as biotic factors in control processes, including in the activity of the nervous system, is still inadequately understood. In particular, their effect on the functional properties of interoceptors, which play in important role in the self-regulation mechanisms of the organism, has hardly been studied.

In this investigation the action of vitally important elements (copper, manganese, and cobalt) was studied on functional properties of the chemoreceptors of the alimentary tract.

EXPERIMENTAL METHOD

Experiments were carried out on 82 adult male cats superficially anesthetized with urethane (1 g/kg intraperitoneally).

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For most experiments a technique of perfusion of the isolated organs was used [7]. The small intestine (except the duodenum and adjacent part of the jejunum), isolated from the circulatory system of the animal, was perfused with oxygenated Tyrode solution heated to 37-38°C, of the following composition: NaCl 0.9%, KCl 0.02%, $NaHCO_3$ 0.001%, $CaCl_2$ 0.02%, $MgCl_2$ 0.01%, NaH_2PO_4 0.005%, glucose 1 g/liter. The innervation of the intestine was left intact. A chemical stimulus (acetylcholine) was applied to the receptors of the loop of intestine through a cannula introduced into the superior mesenteric artery and was flushed out by the flow of perfusion fluid through the superior mesenteric vein. Reflex changes in blood pressure and respiration arising under these circumstances were recorded in the usual way on a kymograph. The state of excitation of the receptors was tested by measuring the intensity of the vascular reflexes to acetylcholine before, during, and after the addition of cuprous, manganous, or cabaltous chloride to the perfusion fluid. The experiments of this series were carried out on 54 animals.

In some experiments (on 28 animals) local application was used: Gauze swabs soaked in a 0.001 M solution of cuprous, manganous, or cobaltous chloride were applied to the gastric mucosa (for 1-3 min), or the stomach was irrigated with the same solutions.

EXPERIMENTAL RESULTS

Application of acetylcholine (10 μg) to the chemoreceptors of the small intestine, isolated from the general circulation, evoked a pressor response and an increase in the frequency and depth of respiratory movement, in agreement with data in the literature [4, 8].

Perfusion of the loop of intestine with 10^{-4} M cuprous chloride solution caused a very small rise of blood pressure which was not statistically significant. However, after preliminary (for 1 min) perfusion of the intestine with cuprous chloride solution the responses of the blood pressure to acetylcholine were completely reversed: Instead of a rise of blood pressure of 11.6 ± 1.16 mm Hg, or 10.5% of the initial level ($P < 0.01$), observed in the control experiments, there was a statistically significant fall of blood pressure by 12.3 ± 1.39 mm Hg, or 10.8% ($P < 0.001$). Application of cuprous chloride solution (0.001 M) to the gastric mucosa caused a transient rise of blood pressure.

Preliminary (for 1 min) perfusion of the intestine with manganous chloride solution (10^{-5} M) potentiated the vascular responses to acetylcholine appreciably: The blood pressure rose on the average by 22.2 ± 1.41 mm Hg, or by 21.2% (before perfusion with the manganese solution by 12.7 ± 1.32 mm Hg, or by 11.5%; $P < 0.001$). Changes in respiration in this case were not significant. Local application of manganous chloride (0.001 M) to the gastric mucosa did not lead to any appreciable changes in the blood pressure or respiration at any time during exposure.

Perfusion (for 1 min) of the loop of intestine with cobaltous chloride solution (10^{-5} M) caused a very slight fall of blood pressure. After the action of cobalt the pressure responses of the blood pressure to acetylcholine were distinctly weakened. The blood pressure rose by only 9.6 ± 1.69 mm Hg, or by 8.8% (before perfusion of the intestine with cobalt by 19.8 ± 5.63 mm Hg, or by 17.4%; $P < 0.02$). In these experiments the latent period of the blood pressure reflexes was characteristically increased by more than threefold. Respiratory movements were slowed and their amplitude reduced. Local application of cobaltous chloride solution (0.001 M) to the gastric mucosa caused the blood pressure to fall.

In a special series of experiments the role of SH compounds in the mechanisms of reception of these trace elements was studied. A single injection of 5% unithiol solution (0.1 ml/kg) into the vessels of the perfused loop of intestine after perfusion with copper or cobalt solution restored the pressor reflexes to acetylcholine. In the experiments with manganese unithiol did not change the course of the reflex responses observed in the presence of magnesium ions.

Blocking SH groups with copper and cobalt thus substantially disturbed the process of chemoreception of acetylcholine.

Changes in the various stages of metabolism in the receptive field of the intestine through interaction between trace elements and thiol groups of specific proteins of the afferent systems may therefore be one cause of the changes in the reflex response of the animal's blood pressure and respiration.

Since the experimental conditions were such that the chemical agent had a local action, strictly confined to the tissues of the perfused organ, the changes observed in the interoceptive reflexes can be assumed to depend mainly on processes taking place in the receptive field of the small intestine itself, i.e., in the peripheral part of the viscerochemical analyzer. Under the influence of copper and cobalt the excitability of the interoceptors is depressed as a result of a disturbance of their metabolism; manganese, on the other hand, increases receptor excitability with the result that reflex responses of the blood pressure and respiration of acetylcholine are potentiated. This conclusion is supported by data in the literature showing that copper and manganese ions had opposite effects on the functional state of the nervous system [5, 6].

LITERATURE CITED

1. G. A. Babenko, Trace Elements in Experimental and Clinical Medicine [in Russian], Kiev (1965).
2. A. O. Voinar, The Biological Role of Trace Elements in Animals and Man [in Russian], Moscow (1960).
3. V. V. Koval'skii, in: Trace Elements in the Life of Plants and Animals [in Russian], Moscow (1952), pp. 55-70.
4. V. A. Lebedeva, Mechanisms of Chemoreception [in Russian], Moscow–Leningrad (1965).
5. V. S. Raitses, Zh. Nevropat. Psikhiatr., No. 1, 128 (1965).
6. V. S. Raitses, in: Proceedings of the First All-Union Scientific Conference [in Russian], Ivano-Frankovsk (1969), pp. 241-243.
7. V. N. Chernigovskii, Afferent Systems of Internal Organs [in Russian], Kirov (1943).
8. V. N. Chernigovskii, Interoceptors [in Russian], Moscow (1960).