EFFECT OF MEDIATORS ON BRAIN TISSUE LEVELS OF SOLUBLE THIOLS

V. N. Gurin

UDC 612.822.1:547.269.1-06:612.822.2

Experiments on albino mice revealed a decrease in the brain tissue level of soluble thiols after administration of arecoline, benzactyzine, and reserpine and an increase in its level after administration of amphetamine and DOPA. Nicotine, pediphen, and 5-hydroxytryptophan had no appreciable effect on the brain tissue level of soluble thiols. It is postulated that catecholamines and acetylcholine, the latter acting on muscarine-like cholinergic systems, play an important role in the regulation of thiol metabolism in the brain.

The study of the mechanisms of nervous regulation of the structure and functions of the organism has shown that mediator processes, especially those of a cholinergic type, are intimately linked with the state of the tissue sulfhydryl groups [3, 4, 8, 9]. In recent years the problem of unity and interconnection of cholinergic and adrenergic processes and of thiol metabolism has been studied [6, 10]. There are reports in the literature that the concentration of thiol compounds in the brain tissue of animals increases after electrical stimulation of the hypothalamus [1], in electric shock [7], and under the influence of general anesthetics and sedatives [2] and of repeated injections of amphetamine [11] and that it falls immediately after injection of ganglion-blocking drugs [5]. However, the effect of the most important mediators of the nervous system on thiol metabolism of the brain has not yet been studied.

This paper gives details of changes in the level of soluble thiols in the brain tissue of mice as a result of interference with their metabolism by acetycholine, catecholamines, and serotonin.

EXPERIMENTAL METHOD

Experiments were carried out on 120 male albino mice weighing 20-25 g deprived of food for 12 h. All drugs were injected intraperitoneally: arecoline (25 mg/kg), nicotine (5 mg/kg), benactyzine (10 mg/kg), pediphen (50 mg/kg), amphetamine (10 mg/kg), DOPA (100 mg/kg), 5-hydroxytryptophan (50 mg/kg), and reserpine (5 mg/kg). The animals were killed by decapitation 15 min after injection of arecoline, amphetamine, and DOPA; 5 min after nicotine; 40 min after benzactyzine, pediphen and 5-hydroxytryptophan; and 12 h after reserpine. The brain was homogenized in the cold in 4 ml of Tris $-HNO_3$ buffer, pH 7.4 (0.01 M Tris $-$ 0.05 N HNO_3) containing EDTA in a concentration of 6×10^{-5} M. Extraction continued for 40 min at 4°C, after which the homogenate was centrifuged. The concentration of total sulfhydryl groups in the supernatant was determined by the method of Benesh et al. [14].

EXPERIMENTAL RESULTS

In the mice of the control group the brain tissue level of soluble thiols was 3.82 ± 0.18 meq/g dry weight of tissue. The muscarine-like cholinomimetic arecoline and the central muscarine-like cholinolytic benactyzine lowered this level, while nicotine and the central nicotine-like cholinolytic pediphen had no effect on it (Fig. 1). The brain tissue thiol concentration was increased after administration of amphetamine, which liberates catecholamines and serotonin, and of the catecholamine precursor DOPA, but was unchanged after injection of 5-hydroxytryptophan, the precursor of serotonin; reserpine lowered the brain tissue thiol level.

Department of Normal Physiology, Minsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. S. Il'in.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 75, No. 4, pp. 42-44, April, 1973. Original article submitted February 7, 1972.

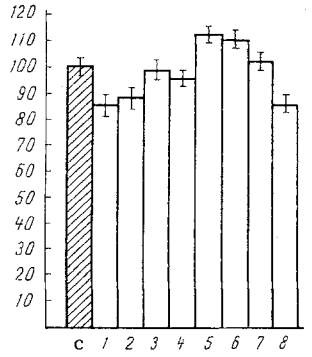

Fig. 1. Change in concentration of soluble thiols (in %) in mouse brain tissue after administration of: 1) arecoline (25 mg/kg);2) benzactyzine(10 mg/kg); 3) nicotine (5 mg/kg); 4) pediphen (50 mg/kg); 5) amphetamine (10 mg/kg); 6) DOPA (100 mg/kg); 7) 5-hydroxytryptophan (50 mg/kg); 8) reserpine (5 mg/kg); C) control.

These results, which indicate that serotonin has no marked effect, suggest that acethylcholine, with a muscarine-like effect, and catecholamines play the most important role in the functional system regulating thiol metabolism in the brain tissue. The absence of any marked effect of nicotine may be because of the narrower distribution of nicotine-like cholinergic systems in the CNS and also because nicotine, unlike arecoline, causes no significant increase in the acetylcholine concentration in the brain tissue during the first 15 min after injection [15]. The results are in harmony with the existing views that the effects of adrenergic and cholinergic systems of the brain may be complementary in character, but are also antagonistic [12, 13, 17]. One of the manifestations of this antagonism, according to the experimental evidence, is their opposite effect on the level of soluble thiol compounds in the brain tissue. The fact that arecoline and benactyzine were found to act in the same direction evidently agrees with results obtained by other workers [16] who found that both benactyzine and cholinesterase inhibitors depress the oxygen consumption of the brain tissue. Assuming that the state of the thiol compounds may be directly dependent on the level of energy metabolism in the nerve cells, the presence of a neuro-hormonal system (acetylcholine–catecholamines) can be postulated in the brain controlling metabolism of the brain and its functional state through the intermediary of thiol compounds.

LITERATURE CITED

1. É. F. Gerasimovich, Byull. Éksperim. Biol. i Med., No. 7, 46 (1969).
2. V. F. Dunaeva and E. F. Ivanenko, Farmakol. i Toksikol., No. 1, 22 (1963).
3. Kh. S. Koshtoyants, Proteins, Metabolism, and Nervous Regulation [in Russian], Moscow (1951).
4. Kh. S. Koshtoyants, Enzyme Chemistry of Excitation and Inhibition and the Evolution of Functions of the Nervous System [in Russian], Moscow (1963).
5. Ya. Z. Lemberskii and M. L. Tarakhovskii, Farmakol. i Toksikol., No. 6, 732 (1964).
6. T. G. Putintseva and T. M. Turpaev, in: Physiology and Biochemistry of Biogenic Amines [in Russian], Moscow (1969), p. 40.
7. O. A. Smirnova, in: Proceedings of the 4th Tbilisi Conference of Physiologists, Pharmacologists, and Biochemists [in Russian], Vol. 2, Saratov (1966), p. 224.
8. T. M. Turpaev, Biokhimiya, No. 4, 456 (1955).
9. T. M. Turpaev, The Mediator Function of Acetylcholine and the Nature of the Cholinergic Receptor [in Russian], Moscow (1962).
10. T. M. Turpaev and B. N. Manukhin, Proceedings of the 5th All-Union Conference on Neurochemistry of the Nervous System [in Russian], Tbilisi (1970), p. 345.
11. D. G. Uzbekova, in: Proceedings of the 4th Volga Conference of Physiologists, Pharmacologists, and Biochemists with the Participation of Morphologists and Clinicians [in Russian], Vol. 2, Saratov (1966), p. 75.
12. V. C. Abrahams and M. Pickford, J. Physiol. (London), 121, 712 (1956).
13. J. L. Barker, J. W. Crayton, and R. A. Nicoll, Science, 171, 208 (1971).
14. R. E. Benesh, H. A. Lardy, and R. Behesh, J. Biol. Chem., 216, 263 (1955).
15. B. Holmstedt, Ann. New York Acad. Sci., 144, 433 (1967).
16. R. Iovic and M. Milosevic, Europ. J. Pharmacol., 9, 304 (1970).
17. A. S. Marazzi and E. R. Hart, Science, 121, 365 (1955).