INCORPORATION OF ACETATE AND PHOSPHATE INTO BRAIN LIPIDS DURING BLOCKING OF CHOLINERGIC AND ADRENERGIC RECEPTORS

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Benactyzine (blocking M-cholinergic receptors) inhibits the incorporation of acetate and phosphate into brain lipids; haloperidol (blocking α-adrenergic receptors) activates these processes. On this basis it is postulated that the conduction of the nervous impulse in cholinergic and adrenergic synapses of the brain is accompanied by changes in the intensity of lipid synthesis.

KEY WORDS: brain; lipid synthesis; blocking of cholinergic and adrenergic receptors.

Acetylcholine and its analog carbachol stimulate the incorporation of inorganic phosphate and inositol into lipids of the whole brain, slices of the cerebral cortex, and nerve endings [5, 7, 9, 10, 12, 13]. The effect of another mediator of the CNS – noradrenalin – on lipid synthesis in brain slices is twofold [6]. Meanwhile, its pharmacological analog amphetamine has no effect on the incorporation of inositol into brain lipids [11]. Investigation of the effect of antagonists of mediators blocking synaptic transmission may help to solve the problem of whether the changes in lipid synthesis in the nerve cells are connected with this process.

The effect of the cholinolytic benactyzine [1, 2] and the adrenolytic haloperidol [8] on the incorporation of acetate and phosphate into rat brain lipids was studied.

EXPERIMENTAL METHOD

Experiments were carried out on female albino rats weighing 200-250 g. Aqueous solutions of benactyzine and haloperidol were injected intraperitoneally in doses of 1 and 0.0025 mg/100 g body weight in a volume of 0.1 ml (the control animals received water). Sodium acetate-1-C^{14} (20 μCi/100 g) or $KH_2P^{32}O_4$ (50 μCi/100 g) was injected intramuscularly at the same time. The animals were decapitated 30 min later. In experiments in which benactyzine was injected, the cerebral cortex was removed, whereas in the experiments with haloperidol the whole forebrain was taken. The fraction of lipids [4], containing all components except polyphosphoinositides and gangliosides, was extracted. The radioactivity of the lipids and of the dry powder of the brain homogenate was measured on a glas-flow counter. The relative specific radioactivity [(specific activity of lipids)/(specific activity of homogenate)] × 100 was used as the measure of the intensity of incorporation of acetate and phosphate.

EXPERIMENTAL RESULTS AND DISCUSSION

Benactyzine lowered the incorporation of acetate and phosphate into the brain lipids (Table 1), practically by an equal degree. Haloperidol had the opposite action: the intensity of lipid synthesis was increased. In this case the incorporation of acetate was activated a little more than that of phosphate.

After blocking of the adrenergic receptors in the brain the process of lipid synthesis was thus intensified. According to the pharmalogical classification haloperidol blocks α-adrenergic receptors, the

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TABLE 1. Incorporation of Acetate and Phosphate into Rat Brain Lipids under the Influence of Benactyzine and Haloperidol (M ± m)

Substance	Statistical index	Acetate		Phosphate	
		control	expt.	control	expt.
Benactyzine	n	19	16	8	7
	$M \pm m$	47±2	37±2	7,7±0,4	6,2±0,5
	P	<0,005		<0,05	
Haloperidol	n	6	5	6	6
	$M \pm m$	41±4	54±4	3,7±0,3	4,5±0,2
	P	<0,02		<0,05	

predominant form among the adrenergic receptors of the brain, and inhibitory from the electrophysiological point of view [3]. Interaction of haloperidol with these receptors must lead to the abolition of their inhibitory function and, as was pointed out above, this is accompanied by activation of lipid synthesis.

Blocking the cortical M-cholinergic receptors leads to a reduction in the intensity of lipid synthesis. This decrease correlates with the electrophysiological inhibition observed with the dose of benactyzine used [1].

The inhibition of lipid synthesis by benactyzine and activation of this process by haloperidol suggest that interaction between acetylcholine and M-cholinergic receptors activates lipid synthesis in the neurons, whereas interaction between noradrenalin and α-adrenergic receptors inhibits this process.

LITERATURE CITED

1. P. P. Denisenko, Central Cholinolytics [in Russian], Leningrad (1965).
2. S. G. Kuznetsov and S. N. Golikov, Synthetic Atropine-like Substances [in Russian], Leningrad (1962).
3. N. A. Losev and Yu. S. Borodkin, Farmakol. i Toksikol., 35, 549 (1972).
4. J. Folch, M. Lees, and G. H. Sloane-Stanley, J. Biol. Chem., 226, 497 (1957).
5. R. O. Friedel and S. M. Schanberg, J. Pharmacol. Exp. Ther., 183, 326 (1972).
6. M. R. Hokin, J. Neurochem., 16, 127 (1969).
7. L. E. Hokin and M. R. Hokin, J. Biol. Chem., 233, 818 (1958).
8. P. A. Janssen, Internat. J. Neuropsychiat., 3, Suppl. 1, 10 (1967).
9. E. G. Lapetina and R. H. Michell, Biochem. J., 126, 1141 (1972).
10. W. L. Magee, J. F. Berry, K. P. Strickland, et al., Biochem. J., 88, 45 (1963).
11. R. U. Margolis and A. Heller, J. Pharmacol. Exp. Ther., 151, 307 (1966).
12. J. Schacht and B. W. Agranoff, J. Biol. Chem., 247, 771 (1972).
13. Y. Yagihara and J. N. Hawthorne, J. Neurochem., 19, 355 (1972).