THE EFFECT OF BENACTISINE ON THE SEROTONIN CONCENTRATION IN CERTAIN PARTS OF THE CAT'S BRAIN

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The investigations of several workers [1, 4, 7] of the depressing action of benactisine on monoamine oxidase, and also the researches of Vojtechovsky and collaborators [8] have shown that the effect of this drug is to decrease the excretion of 5-hydroxyindolacetic acid in the human urine, from which it seems that benactisine and, possibly, certain other central cholinolytics, if given in large doses causing marked disturbances of cerebral activity, may also affect serotonin metabolism. The object of the present investigation was to study the action of benactisine on the serotonin concentration in various parts of the cat's brain.

EXPERIMENTAL METHOD

The serotonin concentration was determined by the biological method of Amin and co-workers [2], based on the property of serotonin to cause contractions of smooth muscle, but with a slight modification: a combination of acetone and heptane was used to extract serotonin from the brain tissue, giving an increased yield.

After removal of the residue by filtration, the solvents were removed from the samples by evaporation in vacuo at a temperature of 34-35°. The dry residue was dissolved in Ringer's solution [5] and the serotonin concentration determined. The rat's colon was used as test object, and 5-hydroxytryptamine creatinine-sulfate as a standard.

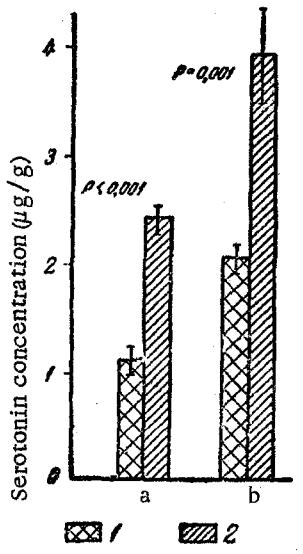

Fig. 1. Effect of iproniazid on the serotonin concentration in the thalamus (a) and hypothalamus (b) of the cat. 1) Animals of the control group. 2) animals of the experimental group.

EXPERIMENTAL RESULTS

Three series of experiments were undertaken (not less than 10 control and 15 experimental cats in each series). The first (control) series of experiments had the object of assessing the sensitivity of the method which we selected for determining the serotonin concentration in the brain tissue. In the first part of this series the serotonin concentration was determined in the thalamus—1.3 μg/g of tissue, and in the hypothalamus—2.1 μg/g of tissue, corresponding to data in the literature [3]. In the same series of experiments the effect of iproniazid on the serotonin concentration in the thalamus and hypothalamus was investigated. This compound was injected intraperitoneally into the cats in a dose of 100 mg/kg, 24-36 h before the determination of the serotonin concentration. After the injection of iproniazid, the serotonin concentration in the thalamus and hypothalamus was increased on the average by 85% (Fig. 1), which also agrees with the data in the literature [6]. Hence, our chosen method was perfectly suitable for determining the serotonin concentration in brain tissue.

The second series of experiments showed that benactisine in small doses (in concentrations of 10^{-9} to 10^{-5}) depressed or even completely prevented the action of serotonin on the intestine. Because of these findings, and also of the fact that benactisine was not completely excreted during the 12 h after its administration, so that its presence in the brain extracts might affect the ability of the intestine to react to serotonin, all subsequent experiments to determine serotonin quantitatively were carried out 24 h after injection of benactisine.

In the third series of experiments we studied the effect of benactisine on the serotonin concentration in the thalamus and hypothalamus. Benactisine was injected subcutaneously in a dose of 1 or 10 mg/kg. These doses were chosen because in doses of 1 mg/kg or over, benactisine causes obvious disturbances of the activity of the nervous system. The results of this series of experiments are shown in Fig. 2. In the experimental group of cats, after administration of 1 mg/kg of benactisine, the serotonin concentration was slightly higher than in the control animals, although this difference was not statistically significant for this number of experiments. When the dose of benactisine was increased to 10 mg/kg a marked increase in the serotonin concentration in the cat's brain was observed: by 40% in the thalamus and by 27% in the hypothalamus.

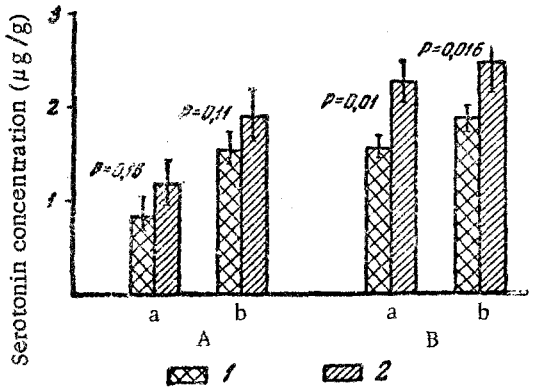

Fig. 2. Effect of benactisine, injected in doses of 1 mg/kg (A) and 10 mg/kg (B), on the serotonin concentration in the thalamus (a) and hypothalamus (b) of cats. (Legend as in Fig. 1).

The mechanism of action of benactisine is probably based on its ability to depress monoamine oxidase [1].

Hence, besides the acti-acetylcholine action of benactisine and, probably, of other central cholinolytics, its effect on other noncholinergic systems must be borne in mind, notably on systems connected with the metabolism of serotonin and possibly of the catecholamines.

SUMMARY

A study was made of benactisine action on serotonin content of some portions of cat brain. As demonstrated, high doses of benactisine affected serotonin metabolism in the brain, increasing the content of this substance.

Evidently, the capacity of benactisine to depress monoaminoxidase lies at the basis of its action mechanism.

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