CHANGES IN BIOGENIC AMINE CONTENT IN VARIOUS PARTS OF THE RAT BRAIN AFTER ADMINISTRATION OF MORPHINE AND AMOBARBITAL

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The effect of narcotics with different chemical structure (morphine and amobarbital) on the concentrations of dopamine, noradrenalin, serotonin, and its principal metabolite 5-hydroxyindoleacetic acid was investigated in various brain structures in rats. The effects of morphine and amobarbital on the biogenic amine system of the brain were found to depend on the time of their action. Changes produced by the narcotics in catecholamine and indoleamine metabolism differed in the hypothalamus, midbrain, and cortex. Responses of the biogenic amine systems were most marked 60 min after administration of the narcotics.

KEY WORDS: biogenic amines; morphine; amobarbital; 5-hydroxyindoleacetic acid; narcotics.

Information has recently been published that an important role in the mechanism of the central action of narcotics is played by their influence on brain biogenic amine metabolism [1-3, 5, 8].

However, the effect of narcotics on the biogenic amine system has been studied only in the whole brain or in the corpus striatum. Moreover, the effects of narcotics have been studied at different times after administration of a single dose, and this could account for the inconsistency of the results.

The object of this investigation was to study the dynamics of the action of narcotics with different chemical structure (morphine and amobarbital) on the levels of catecholamines – dopamine (DA), noradrenalin (NA), serotonin (5-HT), and the principal product of serotonin metabolism, 5-hydroxyindoleacetic acid (5-HIAA) – in the hypothalamus, midbrain, and cerebral cortex of rats.

EXPERIMENTAL METHODS

Experiments were carried out on male Wistar rats weighing 180-200 g. Morphine was injected in a dose of 15 mg/kg and amobarbital in a dose of 35 mg/kg intraperitoneally. The rats were decapitated after 10, 30, 60, and 180 min and the hypothalamus, midbrain, and temporal lobes of the cortex were removed. The concentrations of NA, DA, 5-HT, and 5-HIAA were determined by the method described in [4, 6, 7]. Fluorescence was measured on the Hitachi MPF-2a spectrofluorometer. The experimental results were subjected to statistical analysis by Student's t-test.

EXPERIMENTAL RESULTS AND DISCUSSION

The concentrations of biogenic amines and 5-HIAA (in μg/g wet weight of tissue) in the various parts of the brain of intact animals were as follows: in the midbrain: DA) 1.1 ± 0.08, NA) 0.91 ± 0.05, 5-HT) 0.7 ± 0.09, 5-HIAA) 0.8 ± 0.09; in the hypothalamus: DA) 1.3 ± 0.05, NA) 0.88 ± 0.07, 5-HT) 0.87 ± 0.08, 5-HIAA) 0.64 ± 0.05; cortex: DA) 0.92 ± 0.09, NA) 0.19 ± 0.03, 5-HT) 0.27 ± 0.02, 5-HIAA) 0.22 ± 0.03.

In the initial periods of action of morphine, a rise in the DA level and a fall in the NA concentration in the hypothalamus were observed. Amobarbital caused a small increase in the NA concentration accompanied by a decrease in the DA concentration in this part of the brain. From the 30th to the 60th minutes a sharp decrease was observed in the concentrations of catecholamines under the influence of both narcotics. By the 180th minute the neuromediator level had moved significantly toward the control level after injection of morphine, whereas the effect of amobarbital was still clearly manifested at this time.

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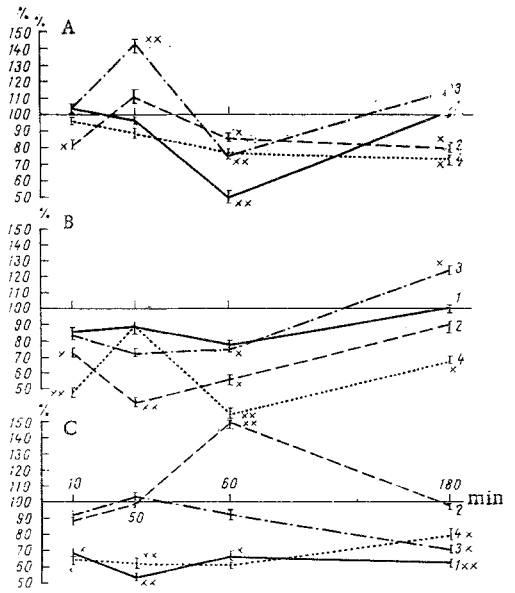

Fig. 1. Changes in concentrations of NA (1, 2) and DA (3, 4) in hypothalamus (A), midbrain (B), and cortex (C) after injection of morphine (1, 3) and amobarbital (2, 4). Ordinate, concentration of catecholamines in % of control; abscissa, time after injection of drugs. (Each point on graph represents mean value of results obtained in 12 animals.) X) $P < 0.05$; XX) $P < 0.01$.

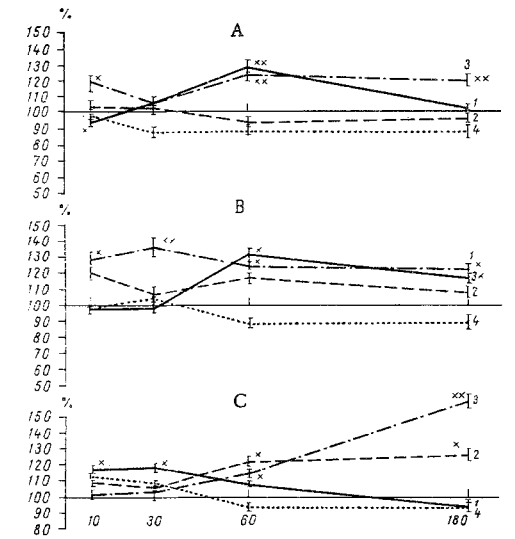

Fig. 2. Change in concentrations of 5-HT (1, 2) and 5-HIAA (3, 4) in hypothalamus (A), midbrain (B), and cortex (C) after injection of morphine (1, 3) and amobarbital (2, 4). Legand as in Fig. 1.

The catecholamine level in the midbrain of the experimental animals fell 10 min after injection of both narcotics, and the greatest decrease occurred after 30-60 min. The catecholamine concentration then increased and regained the control level after 180 min. However, the DA concentration remained significantly below normal after injection of amobarbital.

In the cortex, morphine caused a sharp decrease in the NA and DA concentrations by the 60th minute of its action, which was still detectable by the 180th minute. Amobarbital also led to a marked decrease in the DA concentration in the cortex, whereas the NA level was increased from the 10th to the 60th minutes, returning to normal by the 180th minute. Changes in the NA and DA levels under the influence of the narcotics are shown in Fig. 1.

Clearly, therefore, the effect of the narcotics of the NA and DA concentrations depended on the time of their action. The greatest changes in the DA and NA concentration in the hypothalamus and midbrain were observed 60 min after injection of both morphine and amobarbital. The normal NA and DA levels were restored in the hypothalamus 3 h after the action of morphine, but they remained low in the cortex. Changes in the DA and NA levels caused by injection of amobarbital still persisted after 180 min of the experiment.

The difference in the direction of changes in the concentrations of NA and its precursor in the chain of catecholamine synthesis, namely DA, in the initial stages (10-30 min) of morphine and amobarbital poisoning are definite evidence that the narcotics exert their effect on dopamine-β-hydroxylase, an enzyme regulating the conversion of DA into NA.

Investigation of the effect of morphine and amobarbital on the concentrations of 5-HT and its principal metabolic product (5-HIAA) demonstrated that morphine led to a fall in the 5-HT and 5-HIAA levels in the hypothalamus by the 60th minute, after which the 5-HT level returned close to normal whereas the 5-HIAA concentration remained high (Fig. 2A).

An increase in the concentrations of 5-HT and 5-HIAA in the midbrain was observed 60 min after injection of morphine and it continued until the end of the experiments. Amobarbital led to an increase in the 5-HT concentration and a decrease in the 5-HIAA concentration in this part of the brain by the 60th minute (Fig. 2B).

In the cortex a sharp increase in the 5-HIAA concentration was observed after injection of morphine and an increase in the 5-HT concentration by the 60th minute after injection of amobarbital (Fig. 2C).

Analysis of these results suggests that morphine causes an increase in the 5-HT turnover in the hypothalamus and midbrain and an increase in indoleamine breakdown in the cortex.

Amobarbital in all probability inhibits 5-HT catabolism in all regions of the CNS studied.

Morphine [2, 9] and other narcotics [10] are known to cause a marked increase in catecholamine turnover in the brain of experimental animals. The decrease in the catecholamine level observed during the first hour of action of morphine may be connected with intensification of the liberation and breakdown of neuromediators. Stimulation of indolamine metabolism after a single injection of morphine has been observed in the rat brain [11, 12], whereas amobarbital caused an increase in the 5-HT level accompanied by a decrease in the 5-HIAA concentration [13].

In the present experiments morphine thus caused activation of catecholamine and indoleamine metabolism by the 60th minute of its action, whereas amobarbital had an inhibitory action on 5-HT breakdown.

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