Effect of drugs with addicting properties on brain catecholamines

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INTRODUCTION

A number of data can be found in the literature concerning the effect of addicting drugs on brain amines, aiming at elucidating their role in the production of dependence and withdrawal syndromes [1-5]. Along the same lines, we have published some results concerning the effects of alcohol [6]; in this study data concerning morphine and amobarbital effects on catecholamines (CA) metabolism are presented.

MATERIALS AND METHODS

The study was carried out on 220 male rats of Wistar derivation, weighing 220-260 g. In acute experiments morphine and amobarbital were injected intraperitoneally in doses respectively of 15 mg/kg and 25 mg/kg. One hour after the administration, the rats were decapitated, proceeding immediately to dissection of cortex, hippocampus, striatum, hypothalamus and midbrain.

Norepinephrine (NE) and dopamine (DA) were determined according to the method of Schlumpf and Coll. [7], normetanephrine (NM) according to Ho and Taylor [8], and homovanillic acid (HVA) according to Myrphy and Coll. [9]. Fluorescence measurements were carried out on Hitachi MPF-2a spectrofotometer.

The results of the investigation were elaborated statistically by Student’s criteria.

RESULTS

Morphine, in the dose of 15 mg/kg, significantly decreased NE only in the midbrain, while DA concentration was decreased in midbrain, hypothalamus and cortex. Morphine induced also a considerable lowering of
Fig. 1. — Effects of morphine on the content in catecholamines and their metabolites of various parts of the rat brain. The drug was administered in doses of 15 mg/kg, one hour before sacrifice (100%: control).

Fig. 2. — Effects of amobarbital on the content in catecholamines and their metabolites of various parts of the rat brain. The drug was administered in doses of 25 mg/kg, one hour before sacrifice (100%: control).
NM in the cortex and a marked increase in midbrain, striatum and especially hippocampus. In all regions of the brain HVA levels were found increased (Fig. 1).

Amobarbital, in the dose of 25 mg/kg, leads to a marked DA decrease in all regions of the brain except the striatum. HVA levels were found increased in the hippocampus, while in the hypothalamus and midbrain were found decreased. NE concentration was significantly lower than the control level in the midbrain; in the other regions it was unchanged, whereas NM level was considerably higher in the midbrain, but lower in the cortex (Fig. 2).

DISCUSSION

The results of the investigation indicate that both drugs have an effect on CA metabolism in different brain regions, though the effect is not equal in different areas of central nervous system. Morphine increases both dopamine and norepinephrine metabolism in the striatum and hippocampus; in hypothalamus only dopamine turnover is increased, while in the midbrain turnover of norepinephrine is enhanced. A high turnover of dopamine in the striatum after morphine injection was reported by Groppe and Kushinsky [3] and by Fuxe and Coll. [10]. The decrease in norepinephrine metabolism in the cortex found in the present experiments coincides with the data of Fuxe and Coll. [10].

Amobarbital increases NE turnover in the midbrain and activates DA metabolism in the hippocampus. It is difficult to explain the character of changes in DA metabolism in hypothalamus and midbrain under amobarbital, since both the neurotransmitter and its metabolite HVA are diminished. Confrontation of the effects of morphine and amobarbital with those of alcohol [6, 11] allows to make some further considerations.

All drugs decrease NE and DA concentration in the midbrain. Simultaneous increase in NM level and decrease in HVA level suggest that this decrease is due to intensification of release and disintegration of NE, accompanied by an accelerated transformation of DA into NE (Fig. 3). Amobarbital and alcohol (which give rise to a similar dependence syndrome) administration evokes similar disturbances in the function of the catecholamine system in the hypothalamus, where intensification of release and breakdown of NE was observed.

This suggests that disorders in the catecholamine neurotransmitters system play an important role in the development of the syndrome of drug dependence.
Summary. — The effect of morphine and amobarbital on catecholamine metabolism in different regions of the rat brain (cortex, hippocampus, striatum, hypothalamus and midbrain) was studied. The investigations showed that drugs of different chemical structures but with common addictive properties evoke the same type of changes in catecholamine metabolism, which are expressed by an intensification of release and disintegration of norepinephrine and by a decrease in dopamine level.

REFERENCES


