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Effects of chlorpromazine on the metabolism of catecholamines in dog brain

H. C. GULDBERG and CELIA M. YATES* (introduced by T. B. B. CRAWFORD), *M.R.C. Unit for Research in Brain Metabolism, University of Edinburgh*

A technique was developed whereby the catecholamines and their metabolites could be estimated in the same brain sample. Using solvent extractions, these compounds were separated from a perchloric acid extract of brain into three groups, namely the acids, the amines and the amino-acids. Homovanillic acid and 3,4-dihydroxyphenylacetic acid were estimated in aliquots of the acid fraction. The amines were separated as their acetylated derivatives, using paper chromatography, eluted and estimated fluorimetrically. A new method, more sensitive than that described in the literature (Carlsson & Waldeck, 1964), was developed for the determination of methoxydopamine.

The analytical method was applied to a study of the effects of chlorpromazine (5 mg/kg and 15 mg/kg intravenously) on the catecholamine metabolism in various areas of the brains of beagle dogs. Two hours after drug administration, the following changes were observed in the caudate nucleus: the dopamine concentration was unaltered by 5 mg/kg and decreased by 15 mg/kg; the levels of homovanillic acid and 3,4-dihydroxyphenylacetic acid were increased by 5 mg/kg and unchanged by 15 mg/kg; the concentration of methoxydopamine fell after both doses of chlorpromazine. Similar changes in the levels of dopamine and its metabolites were observed in the globus pallidus. In those areas of brain containing more noradrenaline than dopamine—the hypothalamus, midbrain, thalamus and hindbrain—the concentration of noradrenaline was increased by both doses of chlorpromazine but there were generally no significant alterations in the concentrations of dopamine and its metabolites.

The main effect of chlorpromazine was considered to be a stimulation of catecholamine synthesis (Carlsson & Lindqvist, 1963). Our results could not, however, be explained entirely on the basis of increased synthesis and it was concluded that chlorpromazine exerted more than one action on the brain amines.

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Influence of drugs on catecholamine metabolism in brain as studied by ¹⁴C-tyrosine

H. NYBÄCK* and G. SEDVALL, *Department of Pharmacology, Karolinska Institute and Psychiatric Clinic, St. Göran's Hospital, Stockholm, Sweden*

Results from clinical and pharmacological investigations indicate that changes in the metabolism of brain monoamines exist in diseases of the central nervous system. Several of the most potent psychotropic drugs have been shown to exert specific actions on mono-