The binding of the neurohypophysial hormones to their carrier protein seems to be loose as they can be separated not only by electrophoresis and counter-current distribution (van Dyke, 1968) but also by gel filtration, dialysis and boiling. Acetone did not inactivate the vasopressor activity of van Dyke protein as the hormone was still bound to the carrier protein. But a simple procedure like boiling which liberated about 30% of the hormone, exposed this amount to the action of acetone, and reduced potency by 40%; the extra 10% was probably inactivated before it could re-establish binding with protein. The inference is that acetone acts on the same amino-group with which the hormone attaches itself to the carrier protein.

The author is grateful to Dr. H. B. van Dyke for advice and for generous supplies of van Dyke protein (Batch No. 1090 C), and to Mr. A. Ganesan for technical assistance.

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March 11, 1970

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Inhibition by *p*-chloroamphetamine of the conversion of 5-hydroxytryptamine to 5-hydroxyindoleacetic acid in rat brain

p-Chloroamphetamine (PCA) causes a lowering of 5-hydroxytryptamine (5-HT) in whole brain of rats (Pletscher, Bartholini & others, 1964; Fuller, Hines & Mills, 1964, 1965). Two possible mechanisms are, the inhibition of 5-HT synthesis, and the release of 5-HT from binding sites in brain. The fact that PCA also lowers 5-hydroxyindoleacetic acid (5-HIAA) concentrations in brain pointed to the first possibility, since releasing agents make 5-HT susceptible to attack by monoamine oxidase and thus raise the 5-HIAA concentration (Roos & Werdinius, 1962). An alternative explanation for the lowered 5-HIAA concentration was proposed (Fuller, 1966) on the basis of the ability of PCA to inhibit the oxidation of 5-HT by brain mitochondria from rats. Based on the *in vitro* potency of PCA as an inhibitor and the concentrations found to be present in the brains of rats given PCA, we suggested that the conversion of 5-HT to 5-HIAA in rat brain might be inhibited. To provide direct evidence for this possibility, we have now examined the metabolism of [^{3}H]5-HT formed from [^{3}H]5-hydroxytryptophan (5-HTP) in rats treated with PCA.

In these experiments, male albino rats, about 150 g, were injected intraperitoneally with saline or with PCA at a dose of 20·6 mg/kg (0·1 mmol/kg). 16 h later the rats were given an intraperitoneal injection of [^{3}H]DL-5-HTP (generally labelled, from Volk Radiochemical Company). A tracer amount of the 5-HTP was injected

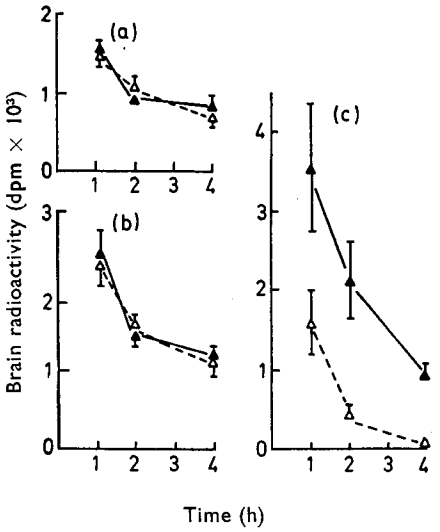

FIG. 1. Radioactive 5-HTP (a), 5-HT (b) and 5-HIAA (c) in whole brain of rats given an i.p. injection of [^{3}H]DL-5-HTP at zero time. Solid lines represent control rats, broken lines are for rats given PCA 16 h before the 5-HTP injection. Means and s.e. for 3 rats per group are shown.

(0·33 mCi/kg; specific activity was 9·1 mCi/mg). Rats were killed by decapitation in groups of three 1, 2 and 4 h later. The brains were rapidly removed and frozen on dry ice. Radioactive metabolites were separated according to the methods of Feldstein & Wong (1965) into fractions containing 5-HTP, 5-HT and 5-HIAA. Radioactivity in each fraction was determined by liquid scintillation spectrometry.

The results are in Fig. 1. At all three time intervals, the amounts of radioactivity present as 5-HTP and as 5-HT were alike in the control and PCA-treated groups. However, the amount of radioactivity present as 5-HIAA was markedly decreased, the differences at the 2 and 4 h intervals being statistically significant ($P < 0.05$). These data strongly suggest that the conversion of radioactive 5-HT to 5-HIAA was decreased and provide direct evidence that inhibition of monoamine oxidase can occur in PCA-treated rats.

Recently, Sanders-Bush & Sulser (1969) have published data indicating that PCA may inhibit the hydroxylation of tryptophan in brain and thus inhibit 5-HT synthesis. Our data do not contradict that possibility.

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April 16, 1970

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