AMPHETAMINE METABOLISM IN AMPHETAMINE-INDUCED PSYCHOSIS

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ELEVEN intravenous abusers of amphetamine were admitted to our clinic in a state of paranoid psychosis, with delusions of persecution, visual and auditory hallucinations and varying degrees of anxiety and motor unrest. All had a history of periodic intravenous abuse of high doses of amphetamine and the presence of amphetamine in their urine was verified in all cases. After admission 6 were given ammonium chloride in order to enhance the urinary elimination of amphetamine, whereas 5 received sodium bicarbonate, by which the excretion of amphetamine is retarded (BECKETT and ROWLAND, 1965). During the first 1–2 days after admission 50 mg of amphetamine were given 3 times daily and during this initial stabilisation period 500 μCi of ^{3}H-*dl*-amphetamine was administered at 8 a.m. Plasma and urine samples were collected during the period of psychosis and the psychotic symptoms were rated 4 times daily (ÄNGGÅRD *et al.*, 1970; JÖNSSON,1972). The radioactive compounds of the urine were separated into four different fractions (ÄNGGÅRD *et al.*, 1973): (1) non-polar bases (mostly amphetamine), (2) polar bases (hydroxylated metabolites), (3) acidic and neutral compounds (deaminated metabolites), (4) watersoluble residue.

It was found that administration of bicarbonate, which retarded the elimination of basic compounds, tended to prolong the course of the psychosis and to intensify the symptoms compared with the group which had an acidic urine. There was an inverse relationship between the urinary output of amphetamine and both basic and deaminated metabolites. Thus, when the pH of urine was high (and the output of amphetamine low) both basic and acidic metabolites increased considerably.

When the ratings of psychotic symptoms were plotted against the plasma levels of amphetamine at 8 a.m. on the second day after admission no correlation was obtained [Fig. 1(a)]. Figure 1(b) shows the relationship between the relative excretion of labelled basic hydroxylated metabolites and psychotic symptoms. Both during conditions of acidic urine (3 cases) and alkaline urine (4 cases) there appeared to be a correlation between the intensity of the psychotic manifestations and the urinary output of hydroxylated metabolites.

The identity of these compounds was established by a series of extraction and ion exchange column procedures in combination with gas chromatography with

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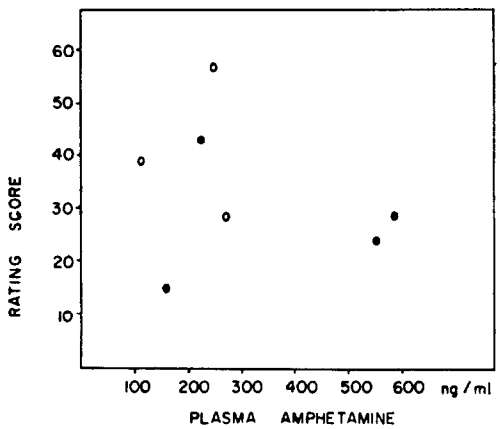

FIG. 1(a).—Plasma amphetamine levels and mean ratings of psychosis during first day after admission.

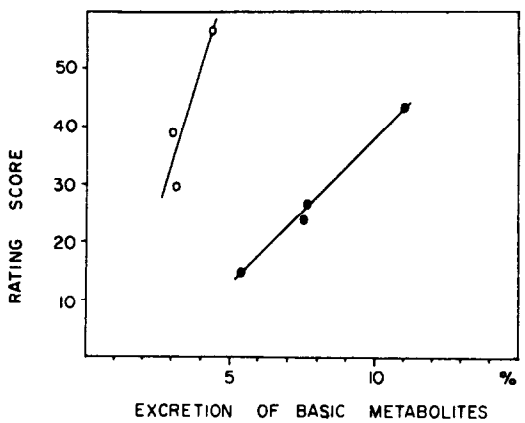

FIG. 1(b).—Relationship between psychosis scores and urinary basic hydroxylated metabolites of amphetamine (expressed as percent of administered ^{3}H-amphetamine). Patients with acidic urine; open circles; alkaline urine: filled circles.

radioactivity monitoring and also by mass spectrometry after conversion into the trifluoroacetyl derivatives. Radioactive peaks were obtained with retention times corresponding to *p*-hydroxyamphetamine, norephedrine and *p*-hydroxynorephedrine. All these compounds give a dominant peak at *m/e* 140 due to a common fragment resulting from cleavage β to the ring. When the mass spectrometer was focused on this fragment, peaks were observed with the retention times of these three metabolites (ÄNGGÅRD *et al.*, 1973). In accordance with SCHWEITZER and FRIEDHOFF (1972), no *p*-methoxyamphetamine could be detected.

A correlation between the intensity of the symptoms of psychosis and the urinary excretion of hydroxylated metabolites may indicate a role for one or more of these metabolites in the production of the psychotic symptoms. The plasma levels of amphetamine on the other hand did not indicate a direct effect of amphetamine on the psychotic manifestations.

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