METABOLIC AND PHYSIOLOGICAL CORRELATES OF THE PSYCHOLOGICAL REACTION TO THREE SHORT-ACTING TRYPTAMINE DERIVATIVES

S. SZARA, L. A. FAILLACE and L. B. SPECK

Clinical Neuropharmacology Research Center, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, D.C., U.S.A.

In vivo animal tests showed that the major metabolite of the hallucinogenic N.N-diethyltryptamine (DET) is 6-hydroxy-N.N-diethyltryptamine (6-HDET) which is excreted mainly as O-glucuronide. N.N-dipropyltryptamine (DPT), another hallucinogenic compound, forms both 6-hydroxy-N.N-dipropyltryptamine (6-HDPT) and 6-hydroxy-N-propyltryptamine (6-HPT), i.e., DPT is dealkylated to a considerable extent while DET is not.

The substitution of the 6-position on the indole ring of DET by a fluoro atom prevents 6-hydroxylation. The resulting compound (6-FDET) is primarily metabolized by dealkylation and oxidation. The major metabolite is 6-fluoroindole-3-acetic acid.

In a series of tests in the same patients metabolic patterns of DET, DPT, and 6-FDET were compared. These patterns were also correlated with the physiological responses (blood pressure, pulse rate, respiration, EEG and evoked cortical potentials) as well as with the psychological reactions observed.

The time course of the autonomic responses closely paralleled the psychological reactions although they usually subsided earlier than some of the psychological effects.

In humans the metabolism of these three compounds followed the same pattern except that DPT was dealkylated better than DET. However, when compared with data obtained from animals, relatively smaller amounts of the 6-hydroxy metabolites of DET and DPT were recovered in the 24 hr postdrug urine sample.

The 6-hydroxylation of DET and DPT is not a major metabolic pathway in man. However this pathway must be important biologically since prevention of 6-hydroxylation (as in the case of 6-FDET) results in a drug which is not psychodysleptic.

Analysis of the human data with the three drugs allows the tentative conclusion that both 6-hydroxylation and dealkylation might be important in producing a psychologically active dysleptic metabolite.

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