Role of tryptaminergic mechanisms in the elements of the behavioural syndrome evoked by tryptophan and a monoamine oxidase inhibitor

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When treated with tryptophan and a monoamine oxidase inhibitor (MAOI), rats develop a syndrome of hyperactivity, hyperreactivity, reciprocal forepaw treading, head weaving, and hind-limb abduction (Hess & Doepfner, 1961). The same syndrome can be produced by the 5-HT releasing drug, *p*-chloroamphetamine. The hyperactivity component of the syndrome is abolished by pre-treatment with *p*-chloro-phenylalanine (Grahame-Smith, 1971). Changes in automatically-recorded activity following tryptophan and MAOI have been used as an index of 5-HT receptor activation, and the interaction of a variety of agents with tryptaminergic mechanisms has been investigated in this way (Green & Grahame-Smith, 1976). Jacobs (1974) has investigated the effects of various treatments on ratings of the individual features of the syndrome, but the results of the two approaches do not always agree. For example, Green & Grahame-Smith (1976) are led by their findings to postulate a dopaminergic link in the production of the syndrome, whereas Jacobs (1974) concludes that the whole syndrome is tryptaminergic.

We have investigated the effects of a 5-HT receptor blocking drug, methergoline (Fuxe, Agnati & Everitt, 1975), on the syndrome using both automated recordings of the hyperactivity and ratings of the individual components of the syndrome. Following the procedure of Grahame-Smith, animals were caged in groups of three, and locomotor activity was automatically recorded with an Animex apparatus. Tryptophan (50 or 100 mg/kg) was administered 30 min after tranylcypromine (10 or 20 mg/kg). *p*-Chloroamphetamine was used to elicit the syndrome in a dose of 10 mg/kg. Methergoline was administered in doses of 2 and 5 mg/kg at the same time as tranylcypromine or 30 min before *p*-chloroamphetamine. Ratings of head weaving, forepaw treading, hind-limb abduction and other components of the syndrome were made by an observer at intervals after drug administration.

Methergoline abolished forepaw treading, head weaving and hind-limb abduction whether elicited by *p*-chloroamphetamine or by tranylcypromine and tryptophan. This striking effect was not paralleled by abolition of the increased activity in either the *p*-chloroamphetamine or tranylcypromine and tryptophan groups. On the contrary, in some groups of animals in which head weaving and forepaw treading had been prevented by methergoline pre-treatment, increased and well-coordinated locomotor activity was observed. Methergoline alone was without effect on locomotor activity.

In summary, a marked qualitative change induced in the tryptophan-MAOI syndrome by 5-HT receptor blockade was not reflected in automated recordings of locomotor activity. This raises doubts as to whether changes in locomotor activity necessarily reflect changes in central tryptaminergic transmission. The results also suggest that different components of the syndrome may have different neurochemical bases.

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