The involvement of 5-hydroxytryptamine and dopamine in the behavioural effects of α-methyltryptamine

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α-Methyltryptamine (α-MT) is an MAO inhibitor that produces a marked behavioural syndrome in rats (Marsden & Curzon, 1977). For the first 60 min after administration (10 mg/kg i.p.) the main features are lateral head weaving, straub tail and hindlimb abduction. This is followed by pronounced and long lasting (4–6 h) running activity with sniffing and rearing. MAO inhibition may account for part of the behavioural response. With other MAO inhibitors, however, the initial behavioural effects are only observed when they are given together with L-tryptophan (Grahame-Smith, 1971). α-MT could stimulate 5-hydroxytryptamine (5HT) receptors directly or indirectly via the release of endogenous 5HT and the present communication studies these possibilities.

α-MT (10 mg/kg i.p.) was given to male Wistar rats caged in pairs and the effects of various drugs on the behavioural response studied. Components of the behavioural response were scored (Marsden & Curzon, 1978) and various types of activity counted using doppler shift radar (King & Marsden this meeting). Pretreatment with p-chlorophenylalanine (150 mg/kg i.p., 24 h) reduced both the behavioural score ($P < 0.001$) and acitvity ($P < 0.001$). Methiothepin (2.5 mg/kg i.p. 30 min before α-MT), which blocks both 5HT and dopamine receptors, significantly reduced the behavioural score ($P < 0.001$) and running activity observed during the second h after injection of α-MT ($P < 0.001$). Methergoline (2 mg/kg i.p.), a specific 5HT antagonist, given 60 min before α-MT reduced the behaviour score ($P < 0.001$) but did not prevent the running activity. Pimozide (0.3 mg/kg i.p., 30 min before α-MT) a specific dopamine antagonist did not significantly alter the behavioural score but reduced the running activity.

Both fluoxetine (10 mg/kg i.p.) and chlorimipramine (12.5 mg/kg i.p.) given 30 min before α-MT significantly reduced the behaviour score. Fluoxetine did not prevent the running activity but delayed its onset and reduced its intensity. Chlorimipramine also significantly reduced ($P < 0.001$) the behaviour score following the administration of the 5HT agonist 5-methoxy-N,N-dimethyltryptamine suggesting chlorimipramine blocks 5HT receptors and 5HT uptake (Buus Lassen, 1978).

The results indicate that both 5HT and dopamine receptors are involved in the behavioural effect of α-MT. The initial effects may be due to the uptake by 5HT neurones of α-MT and the subsequent displacement and release of endogenous 5HT while the running activity appears to involve dopamine and 5HT receptors.

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