Modulation of amphetamine hyperactivity by DPI injected into rat nucleus accumbens

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It has been suggested that dopamine injection into the nucleus accumbens may act on neuroleptic sensitive receptors (designated DAe) to cause a locomotor hyperactivity, and on a second type of receptor (designated DAi) to reduce activity. Ergometrine and (3,4-dihydroxy-phenylamino)-2-imidazoline (DPI) are thought to enhance and reduce activity respectively via this second receptor mechanism (Cools & van Rossum, 1976). However, the dominant effect of dopamine appears to be on the DAe hyperactivity component, and it was considered that a similar system of dopamine receptor stimulation may relate to the hyperactivity induced by (+)-amphetamine.

Bilateral guide cannulae for injections into the nucleus accumbens of male Sprague-Dawley C.F.E. rats, 275–300 g, were chronically implanted using standard stereotaxic techniques (Costall & Naylor, 1976), and drug or vehicle was deposited at Ant. 9.4, Vert. 0.0, Lat. ±1.6 (De Groot, 1959). Locomotor activity was measured in individual perspex cages each fitted with one photocell unit placed off-centre: the number of interruptions of the light beam was recorded every 10 min for a total of 4 hours. (+)-Amphetamine (0.5–2.0 mg/kg i.p.) induced a dose-dependent hyperactivity which persisted for 2–4 hours. 1.5 mg/kg i.p. (+)-Amphetamine was selected as a suitable submaximal dose for use in subsequent studies. An established response to this dose of (+)-amphetamine was antagonised by intra-accumbens injections of fluphenazine (1.0–4.0 μg) and DPI (5–20 μg). An analysis of the antagonistic action of DPI (10 μg) showed that its effect could be reduced or abolished by 30 min pretreatments with cyproheptadine (2.0–5.0 mg/kg i.p.) or methysergide (0.25–1.25 mg/kg i.p.). However, 30 min pretreatments with propranolol (1.25–10 mg/kg i.p.), piperoxan (20 mg/kg i.p.) and atropine (1.0–10 mg/kg i.p.) failed to modify the effects of DPI (5–10 μg): these pretreatments, in addition to methysergide and cyproheptadine, failed to modify the amphetamine hyperactivity *per se*.

It is concluded that whilst amphetamine hyperactivity is known to involve a release of dopamine on to neuroleptic sensitive mechanisms within the nucleus accumbens (present studies; Pijnenburg, Honig & van Rossum, 1975), this mechanism is subject to a direct and/or indirect modulation by a further system which is sensitive to DPI which involves a serotonergic component.

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