A comparison of circling behaviour induced in nigro-striatal lesioned rats after peripheral administration of indole derivatives

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A number of compounds related to tryptamine and three piperidinyl-indole derivatives have been examined for their effects on the circling behaviour in nigro-striatal lesioned rats.

Sprague Dawley rats were electrolytically lesioned in the right striatum (A 8.2, L 3.0, H-0.8) (König & Klippel, 1963) or injected with 6-hydroxydopamine in the right substantia nigra (Ungerstedt, 1971).

The following compounds were tested: tryptamine HCl (10 mg/kg i.p.), 5-methoxytryptamine (5-MT; 5 mg/kg i.p.); 5-methoxy *N*, *N*-dimethyltryptamine (5-MDT; 1 or 2 mg/kg i.p.), (±)-5-hydroxytryptophan (5-HTP; 200 mg/kg i.p.), LSD (0.2 or 1 mg/kg i.p.), methysergide maleate (5 mg/kg s.c.), 3-(4-piperidinyl) 1 H-indole HCl (PI or RU 22424) and the corresponding 5-hydroxy- and 5-methoxy-substituted indole derivatives (5-HPI and 5-MPI or RU 23686), 10 or 20 mg/kg i.p.

In striatal lesioned rats, tryptamine and the 5-substituted derivatives (5-MT, 5-MDT, 5-HTP) were inactive as well as methysergide while LSD caused ipsilateral circling at the high dose used (1 mg/kg). Although PI and 5-HPI had no effect, 5-MPI (10 mg/kg) induced a long lasting contralateral turning behaviour (maximum 3rd h. ipsilateral turns 12 ± 3/contralateral turns 208 ± 26, $n = 36$).

When tested 1 h after scopolamine bromhydrate (10 or 25 mg/kg i.p.) no modification was observed for tryptamine, 5-MT, 5-MDT, and methysergide, while LSD-induced ipsilateral turning was potentiated. In the piperidinyl-indole series scopolamine revealed a strong contralateral rotating behaviour with PI (maximum 3rd h., ipsilateral turns 66 ± 12/contralateral turns 191 ± 22, $n = 22$) similar to the effects of 5-MPI which were prolonged in these conditions.

In nigral lesioned rats the tested compounds were inactive except LSD (0.2 mg/kg) which induced strong contralateral turning and 5-MPI which, at the highest dose only (20 mg/kg) provoked a biphasic response characterized by ipsilateral turning followed by contralateral turning in some animals.

The direction of rotations observed with 5-MPI alone of PI after treatment with a cholinolytic in striatal lesioned rats, and their inefficiency at the same dose in supersensitive 6-hydroxytryptamine lesioned rats are in contradiction to a stimulation of post-synaptic striatal dopamine receptors. Blockade of these receptors is no more likely since PI and 5-MPI do not antagonize apomorphine-induced rotations but on the contrary potentiate them. Moreover there is no clear evidence for a role of tryptaminergic pathways in the mechanism of circling observed with PI and 5-MPI, since 5-HTP, a precursor of 5-HT, and 5-MT or 5-MDT, proposed as 5-HT receptor stimulants do not exhibit any effect in the same experimental conditions.

Just as some experiments have shown that rotations induced by dopamine receptor stimulants were not necessarily the consequence of an impairment in the nigro-striatal tract (Costall & Naylor, 1974; Pycock, Donaldson & Marsden, 1975), the results obtained with the two piperidinyl-indole derivatives clearly suggest that rotations do not solely originate from a classical dopamine receptor stimulating action.

References

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