before propranolol was 1.7×10^{-8} mol, and after propranolol 1.8×10^{-9} mol (for noradrenaline: 3.9×10^{-9} and 2.6×10^{-9} mol respectively).

The vasoconstrictor potency of phenylephrine was unaffected by propranolol.

Whilst the predominant effects of noradrenaline and adrenaline on the hepatic arterial vasculature are vasoconstrictor, a secondary vasodilatation occurs with these catecholamines, but not with phenylephrine. The potentiation of the vasoconstriction and attenuation of the secondary vasodilatation due to the catecholamines by propranolol illustrates the role of β-adrenoceptor stimulation in the responses of this vascular bed to i.a. catecholamines.

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Turning behaviour elicited by apomorphine, (+)-amphetamine and three ergot derivatives in rats treated with a unilateral injection of ethanolamine-*O*-sulphate in the substantia nigra

A.L. JATON, D.M. LOEW & J.M. VIGOURET

Biological and Medical Research Division, Sandoz Ltd., Basle, Switzerland

Recently, Dray, Oakley & Simmonds (1975) have reported that apomorphine and (+)-amphetamine elicit ipsilateral turning in rats which have received a unilateral injection of ethanolamine-*O*-sulphate (EOS) into the substantia nigra. After EOS injection, these animals showed an elevation of GABA concentration in the substantia nigra brought about by an inhibition of GABA transaminase (Fowler, 1973). This may correspond to an activation of an inhibitory GABA-minergic pathway from the striatum to the dopamine containing neurons of the zona reticulata of the substantia nigra (McGeer, McGeer, Wada & Jung, 1971; Kim, Bak, Hassler & Okada, 1971). We wish to report on the effects of three ergot derivatives which have been shown to elicit contralateral turning in rats with a unilateral degeneration of the nigro-striatal pathways after administration of 6-hydroxydopamine into the substantia nigra.

Under nembutal anaesthesia, male OFA rats (250 g) received unilateral injections of EOS (50 µg in 1.5 µl) stereotaxically directed into the zona reticulata of the substantia nigra. Drugs were administered s.c., 24 h after EOS, 6 rats per group. Behaviour was assessed during the following 7 hours. Injection sites were confirmed histologically.

As reported by Dray, Oakley & Simmonds (1975), apomorphine and (+)-amphetamine (1–4 mg/kg) both elicited ipsilateral turning. After 4 mg/kg, the total number of turns was 513 ± 87 and 852 ± 111, respectively. In contrast to the results of Dray, Fowler, Oakley, Simmonds & Tanner (1975), bromocriptine (10 or 50 mg/kg) elicited ipsilateral postural asymmetry and stereotyped sniffing. Ipsilateral turning was only observed upon handling. The ergoline derivative CF 25–397 (Jaton, Loew & Vigouret, 1976) induced only contralateral asymmetry at doses of 20 to 50 mg/kg. LSD–25 (1 or 4 mg/kg) induced typical contralateral turning. After 4 mg/kg, the total number of turns was 210 ± 49.

These results indicate that the three ergot derivatives investigated exert differential actions in EOS treated rats. As opposed to apomorphine and (+)-amphetamine, LSD–25 was the only compound which elicited contralateral turning after unilateral inhibition of GABA metabolism.

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Specificity of monoamine neurotoxins: rotational responses to dopaminergic agonists after unilateral 6-OHDA and 5,6-DHT lesions of the median forebrain bundle

J.L. WADDINGTON
(introduced by T.J. CROW)

Division of Psychiatry, Clinical Research Centre, Harrow, Middlesex HA1 3UJ

The relative specificity of the catecholamine neurotoxin 6-hydroxydopamine (6-OHDA) contrasts with the non-specific degeneration of both 5-hydroxytryptamine (5-HT) and dopamine (DA) neurones induced by the indolamine neurotoxin 5,6-dihydroxytryptamine (5,6-DHT) following intracerebral injection (Saner, Pieri, Moran, Da Prada & Pletscher, 1974). Recent studies suggest that ascending 5-HT neurones may modulate the output of nigrostriatal DA mechanisms. When these effects are investigated using the rotating rat model (Ungerstedt & Arbuthnott, 1970), circling responses to both direct and indirect DA agonists are potentiated by drugs attenuating whole brain 5-HT transmission while treatments enhancing 5-HT transmission decrease such rotation (Milson & Pycock, 1976). To investigate this interaction further, circling responses have been investigated following unilateral depletion of DA and unilateral rather than whole brain depletion of 5-HT induced by injection of neurotoxins into the median forebrain bundle (MFB) (Costall, Naylor & Pycock, 1975).

Male Sprague-Dawley rats, 150 ± 20 g, were given unilateral stereotaxic injections of 6-OHDA) 8 μg/4 μl saline), or 5,6-DHT (5 μg/4 μl saline) into the MFB. Groups of rats from each lesion procedure received i.p. injections of either apomorphine (1 mg/kg) or (+)-amphetamine (5-mg/kg) 8 days after surgery; they were then placed in automated rotometer bowls for continuous recording of all rotations. Rats were sacrificed and striata assayed spectrophotofluorimetrically for DA and 5-HT content 14 days after lesion. Rotations were assessed conventionally and after orthogonal polynomial transformation.

6-OHDA lesions produced an 85.5% depletion of striatal DA ($P < 0.0005$) together with a 28.0% depletion of striatal 5-HT ($P < 0.05$); 5,6-DHT lesions produced a 53.8% depletion of 5-HT ($P < 0.01$) together with a 84.9% depletion ($P < 0.001$) of DA. 6-OHDA lesioned animals showed the expected contralateral and ipsilateral rotation to apomorphine and amphetamine respectively. 5,6-DHT lesioned animals showed more rapid onset of contralateral rotation to apomorphine compared with 6-OHDA lesioned animals ($P < 0.02$), indicating that unilateral depletion of striatal 5-HT produces the same facilitation of apomorphine-induced rotation in unilaterally DA lesioned animals as bilateral depletion of 5-HT; rotational responses to amphetamine after 5,6-DHT lesions, however, were attenuated when compared with 6-OHDA lesions ($P < 0.05$), contrary to the enhancement seen after bilateral 5-HT reduction (Milson & Pycock, 1976). This suggests a 5-HT inhibition of nigrostriatal output which, when reduced by unilateral 5-HT lesion enhances apomorphine effects on the ipsilateral side; this procedure attenuates the effects of amphetamine, which acts on the contralateral side, by enhancing the opponent ipsilateral output.

These results suggest that the influence of 5-HT on DA-dependent rotation is exerted at sites within the striatum rather than on the cell bodies or terminals of the nigrostriatal DA pathway. In addition, they emphasize the non-specificity of the degenerative effects of 6-OHDA and 5,6-DHT on catecholamine and indolamine neurones, especially when applied to densely packed monoamine pathways in the MFB.