Analgesics and rotational behaviour in rats with unilateral substantia nigra lesions. Effects in the presence and absence of (+)-amphetamine

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It has previously been reported that morphine and the narcotic antagonist analgesics, buprenorphine and pentazocine, antagonize apomorphine-induced turning behaviour in rats with lesions (caused by 6-hydroxydopamine) in the left substantia nigra (Cowan, Dettmar & Walter, 1975). The three analgesics have now been tested in the same behavioural model against (ipsilateral) turning evoked by (+)-amphetamine (Ungerstedt, 1971). At least 28 days after surgery, the colony of male Sprague-Dawley rats (initially 180-200 g) was injected with (+)-amphetamine sulphate (2 mg/kg, i.p.). Fifteen minutes later, each rat was individually placed in a 'rotometer' and the incidence of circling was monitored for 50 minutes. The 'rotometer', which displays the number of clockwise and anticlockwise turns of 6 rats over any pre-set time interval of up to 99 min, will be demonstrated.

After at least 7 days, groups of 8-10 rats received s.c. either physiological saline solution or one of a series of doses of buprenorphine, morphine or pentazocine. Fifteen minutes later, the animals were challenged with (+)-amphetamine or saline and, a further 15 min later, the extent of circling was recorded for 50 minutes.

In the absence of (+)-amphetamine, buprenorphine (0.01-0.30 mg/kg), morphine (0.30-3 mg/kg) and pentazocine (1-10 mg/kg) increased ipsilateral turning in a dose-related manner. Smaller increases were obtained with higher doses of buprenorphine (1 mg/kg), morphine (10 mg/kg) and pentazocine (30 mg/kg). Significant differences in turning were obtained, in relation to saline-injected controls, with rats receiving each of the doses of buprenorphine, morphine at 1 and 3 mg/kg and pentazocine at 3, 10 and 30 mg/kg ($P < 0.05$, Mann Whitney U test).

Buprenorphine caused a significant reduction in D-amphetamine-induced turning at 0.10 and 0.30 mg/kg ($P < 0.05$) but not at 0.03 and 1 mg/kg. With morphine (0.03-10 mg/kg) and pentazocine (0.10-30 mg/kg) a significant reduction in turning only occurred with the top dose of each compound ($P < 0.05$).

The ability of the same doses of buprenorphine to both cause turning and antagonize D-amphetamine-induced turning suggests an unusual involvement of this new analgesic with the nigrostriatal system.

References

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Thrombolytic and anti-thrombotic properties of dihomo-γ-linolenate *in vitro*

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Arterial thrombosis is thought to be precipitated by intravascular platelet clumping (Mustard & Packham, 1975) and vasoconstriction could be a complicating factor.

Prostaglandin E_1 (PGE_1 has very desirable actions as a potential anti-thrombotic drug, since it can completely prevent aggregation of platelets induced by large concentrations of any aggregating agent (Kloeze, 1967; Chandra Sekhar, 1970). It thus has advantages over aspirin which can only inhibit that component ('second phase') of the aggregation response that is mediated through enzymatic conversion of platelet arachidonate to prostaglandin endoperoxide (Willis, 1974a, b; Hamberg, Svensson, Wakabayashi & Samuelsson, 1974; Willis, Vane, Kuhn, Scott and Petrin, 1974).

Prostaglandin E_1 has not been used as an anti-thrombotic agent because of its rapid inactivation (Ferreira & Vane, 1967) and expected variety of severe side effects. However, it has recently been proposed that administration of the PGE_1 precursor, dihomo-γ-linolenate (DHLA) might overcome these drawbacks, since PGE_1 would then be produced as required at its site of