The effect of acute doses of buprenorphine on concentrations of homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) in the rat forebrain

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The new narcotic antagonist analgesic, buprenorphine (0.01–1.0 mg/kg, s.c.), induces ipsilateral turning behaviour in rats with lesions (caused by 6-hydroxydopamine) in the left substantia nigra (Cowan, Dettmar & Walter, 1975a). Over the same dose range, buprenorphine antagonizes apomorphine-induced turning in the rat model (Cowan, Dettmar & Walter, 1975b). These effects may be related to an ability of buprenorphine to release dopamine in the central nervous system but an indirect action on noradrenergic or tryptaminergic pathways cannot be excluded. To investigate these possibilities, the concentrations of homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5HIAA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) were simultaneously measured in the forebrains (containing frontal cortex, basal ganglia and hypothalamus) of male Sprague-Dawley albino rats (150–180 g; $n=5$–6) 1 h after injection of buprenorphine hydrochloride (0.1, 3 and 10 mg base/kg, s.c.), haloperidol (0.3, 1 and 3 mg/kg, i.p.), or vehicle (5 ml/kg).

5-Hydroxyindoleacetic acid was measured using the method of Curzon and Green (1970) and MHPG was estimated using a semi-micro method based on the gas-liquid chromatographic procedure of Walter & Eccleston (1973); HVA was estimated using gas liquid chromatography after forming the 4′-trifluoracetyl, trifluorethyl ester of HVA.

Statistically significant increases in the concentration of HVA were obtained after injection of buprenorphine (0.1, 3 and 10 mg/kg, $P<0.01$ by Student's t test) or haloperidol (0.3, 1 and 3 mg/kg, $P<0.01$) however, the concentrations of 5-HIAA and MHPG were not significantly affected by either compound.

Naloxone hydrochloride (3 mg salt/kg, s.c. at −5 min) antagonized the increase in HVA caused by buprenorphine (0.1 mg/kg, $P<0.05$; 3 mg/kg, $P<0.01$) but had no significant effect on the increase in HVA produced by haloperidol (1 mg/kg). At this dose level, naloxone did not significantly alter the concentrations of HVA, 5-HIAA or MHPG. The contrasting results obtained with naloxone are similar to the previous findings (Cowan, Dettmar & Walter, 1975b) that naloxone (3 mg/kg) antagonizes the inhibitory effect of buprenorphine (0.1 mg/kg), but not that of haloperidol (1 mg/kg), on apomorphine-induced turning behaviour in rats.

The present data suggest that doses of buprenorphine which cause behavioural changes may increase the turnover of dopamine, but not that of noradrenaline or 5-hydroxytryptamine, in the forebrain of rats. An opiate link would appear to be involved in the mediation of this effect since the rise in HVA is naloxone-sensitive.

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The stimulated release of dopamine-β-hydroxylase from intact organs of normo- and hypertensive rats

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Measurement of the circulating levels of dopamine-β-hydroxylase (DBH), the mixed function oxidase catalysing the hydroxylation of dopamine to noradrenaline in postganglionic monoaminergic neurones and the adrenal medulla, has been proposed as a useful index of sympathetic nervous activity (Axelrod, 1972). Its application as a means of studying sympathetic nervous involvement in hypertension has not been accepted by all workers (Geffen, Rush, Louis & Doyle, 1973; Horwitz, Alexander, Lovenberg & Keiser, 1973) since the enzyme levels measured in serum from man and