

Studies on the centrally mediated cardiovascular effects of apomorphine in the anaesthetized rat

L. FINCH & A. HERSOM*

School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, BD7 1DP

Apomorphine is a potent dopamine receptor agonist (Anden Rubenson, Fuxe & Hokfelt, 1967; Struyker Boudier, 1975), which on intravenous injection in both cats and rats produces a short lasting fall in blood pressure associated with an intense bradycardia (Barnet & Fiore, 1971; Finch & Haeusler, 1973). These effects are centrally mediated, since a pressor response is obtained in spinalized preparations. More recently Dutta, Guha & Pradhan (1975) found that intraventricular (i.c.v.) apomorphine produced depressor responses in anaesthetized cats, an effect which was not dose related.

In this study we have examined the effect of i.c.v. injections of apomorphine on the resting blood pressure and heart rate in anaesthetized renal hypertensive rats.

Apomorphine (1-100 μ g i.c.v.) caused a short lasting dose related fall in blood pressure and heart rate in the urethane-anaesthetized rat preparation. Pretreatment with fluphenazine (0.5 mg/kg i.p.), haloperidol (0.5 mg/kg i.p.) or metoclopramide (10 mg/kg i.p.) abolished the depressor response to apomorphine (10 μ g i.c.v.), but pretreatment with piperoxan (200 μ g i.c.v. or 10 mg/kg i.p.) did not affect the depressor response to apomorphine (10 μ g i.c.v.). Furthermore atropine (1 mg/kg i.p.) pretreatment abolished the cardiovascular effects of apomorphine (10 μ g i.c.v.).

Pretreatment 3 days earlier with *p*-chlorophenylalanine (400 mg/kg i.p.), which causes depletion of brain 5-hydroxytryptamine levels (Miller, Cox, Snodgrass & Maickel, 1970), did not affect the depressor response to apomorphine (10 μ g i.c.v.).

In renal hypertensive rats, intravenous injections of apomorphine (0.01-1.0 mg/kg i.v.) produced short lasting falls in blood pressure associated with an intense bradycardia. Low doses of apomorphine (0.01-0.1 mg/kg i.v.) could be antagonized by pretreatment with haloperidol (0.5 mg/kg i.v.) or metoclopramide (10 mg/kg i.v.). The highest dose was reduced but not abolished.

These results suggest that central dopamine receptors rather than adrenoceptors or serotonin receptors are involved in the mediation of the central hypotensive action of apomorphine in the anaesthetized rat.

A.H. is the holder of a S.R.C. Studentship in conjunction with Dr B.J. Alps of Wyeth Laboratories.

References

- ANDEN, N.E., RUBENSON, A., FUXE, K. & HOKFELT, T. (1967). Evidence for dopamine receptor stimulation by apomorphine. *J. Pharm. Pharmac.*, **19**, 627.
- BARNETT, A. & FIORE, J.W. (1971). Hypotensive effects of apomorphine in anaesthetized cats. *Eur. J. Pharmac.*, **14**, 206-208.
- DUTTA, S.N., GUHA, D. & PRADHAN, S.N. (1975). Cardiovascular effects of central microinjections of apomorphine in cats. *Arch. int. Pharmacodyn.*, **215**, 259-265.
- FINCH, L. & HAEUSLER, G. (1973). The cardiovascular effects of apomorphine in the anaesthetized rat. *Eur. J. Pharmac.*, **21**, 264-270.
- MILLER, F.P., COX, R.H., SNODGRASS, W.R. & MAICKEL, R.P. (1970). Comparative effects of *p*-chlorophenylalanine, *p*-chloroamphetamine, *p*-chloro-*N*-methyl-amphetamine on rat brain nor-epinephrine, serotonin and 5-hydroxyindole-3-acetic acid. *Biochem. Pharmac.*, **19**, 435-442.
- STRUYKER BOUDIER, H. (1975). Two types of dopamine receptors in the brain of the snail *Helix aspersa*. *Abstracts Sixth Int. Congr. Pharmac. Helsinki*, 1975, p. 487.

The interpretation of responses of motoneurone field potentials to 5-hydroxytryptamine

S. BARASI, O. PARRY & M.H.T. ROBERTS*

Department of Physiology, University College, Cardiff

A previous communication to the society (Barasi & Roberts, 1974a) reported that 5-hydroxy-

tryptamine (5-HT) applied by microiontophoresis in the ventral horn of the rat spinal cord, increased the amplitude of antidromically evoked field potential responses of motoneurons. This response to 5-HT closely resembled the effect on motoneurons of stimulating the raphe nuclei. Comparison of these actions of 5-HT with the effect of intravenously administered L-tryptophan on the dorsal root evoked monosynaptic reflex, suggested that 5-HT may, by an unknown