Noradrenergic influences on dopamine-dependent behaviour in rats

C. PYCOCK

Department of Neurology, Institute of Psychiatry, Denmark Hill, London SE5 8AF

It is difficult to assess the precise neurotransmitter roles of noradrenaline in the brain. It has been suggested that noradrenaline may play a modulator role in the control of motor activity (Andén & Strömbom, 1974), and its action may be facilitation of the nigro-neostriatal dopaminergic system of the brain (Pycock, Donaldson & Marsden, 1975). However, it has been demonstrated that a noradrenergic component is apparently not important for the production of amphetamine-induced locomotor activity (Roberts, Zis & Fibiger, 1975) or stereotyped behaviour (Creese & Iversen, 1975) in rats, although an intact dopamine system is necessary (Creese & Iversen, 1974). Work described here has utilized two animal models with lowered cerebral noradrenaline levels to study the effect on behaviour in rats characteristically observed after dopamine receptor stimulation and dopamine receptor blockade.

Depletion of cerebral noradrenaline was achieved in two separate groups of rats by (i) injection of 6-hydroxydopamine at birth, and (ii) bilateral electrolesions placed in the region of the locus coeruleus in adult rats. When both groups, plus an additional litter-mate control group, had reached adult stage, the intensity of catalepsy induced by the dopamine receptor blocking agent haloperidol (range 0.1–2 mg/kg) was observed. A month later, the stereotyped behaviour induced by both directly and indirectly acting dopamine receptor agonists (apomorphine, 0.1–5 mg/kg s.c., and amphetamine, 0.1–10 mg/kg i.p.) was compared in the 3 animal groups. After a further month, animals were killed for determination of forebrain monoamine levels.

Both 6-hydroxydopamine at birth and bilateral locus coeruleus lesions specifically harmed the dorsal noradrenergic bundle innervation of forebrain structures. Dopamine and 5-hydroxytryptamine levels were not changed. Cortical noradrenaline levels fell to between 40–50% of control levels ($P < 0.001$) for both types of lesions.

Cerebral noradrenaline depletion had no effect on stereotyped behaviour induced by either apomorphine or amphetamine, but it did significantly enhance both the time to onset and intensity of catalepsy induced by haloperidol at all doses used.

It is difficult to comment on the mechanism by which lowered central noradrenaline levels modifies catalepsy, due to apparent dopamine receptor blockade, but does not influence stereotypy resulting from dopamine receptor stimulation. It is possible that two different populations of dopamine receptor are responsible for the two types of behaviour, and that each is modified by different noradrenergic mechanisms.

(C.P. is a Fellow of the Parkinson's Disease Society.)

References

ANDEN, N-E. & STRÖMBOM, U. (1974). Adrenergic receptor blocking agents: effects on central noradrenaline and dopamine receptors and on motor activity. *Psychopharmac. (Berl.)*, **38**, 91–103.

CREESE, I. & IVERSEN, S.D. (1974). The role of forebrain dopamine systems in amphetamine-induced stereotyped behaviour in the rat. *Psychopharmac. (Berl.)*, **39**, 345–357.

CREESE, I. & IVERSEN, S.D. (1975). The pharmacological and anatomical substrates of the amphetamine response in the rat. *Brain Res.*, **83**, 419–436.

PYCOCK, C.J., DONALDSON, I.MacG. & MARSDEN, C.D. (1975). Circling behaviour produced by unilateral lesions in the region of the locus coeruleus in rats. *Brain Res.*, **97**, 317–329.

ROBERTS, D.C.S., ZIS, A.P. & FIBIGER, H.C. (1975). Ascending catecholamine pathways and amphetamine-induced locomotor activity: importance of dopamine and apparent non-involvement of norepinephrine. *Brain Res.*, **93**, 441–454.

Paradoxical aversive property of dexamphetamine

D.A. BOOTH, G. D'MELLO, C.W.T. PILCHER & I.P. STOLERMAN

MRC Neuropharmacology Unit and Department of Psychology, University of Birmingham.

The intravenous self-administration of dexamphetamine shows that it can serve as a reinforcer in rats (Pickens & Thompson, 1971) but a paradoxical, aversive property has been observed with oral self-administration (Le Magnen, 1969; Stolerman, Kumar & Steinberg, 1971). Rats have also been shown to reject distinctively flavoured solutions when their previous consumption was followed by intraperitoneal dexamphetamine (Cappell & LeBlanc, 1971), and a modified procedure involving discrimination between two flavours has been used to analyse further the aversive action of the drug.