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Interaction of clonidine with dopamine-dependent behaviours in rodents

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The central pharmacology of clonidine (2-(2,6-dichlorophenylamino)-2-imidazoline) is complex. It is generally believed to stimulate central α-adrenoceptors (Andén, Corrodi, Fuxe, Hökfelt, Hökfelt, Rydin & Svensson, 1970), although more recent work suggests that it may also modulate central tryptaminergic mechanisms (Maj, Mogilnicka & Palider, 1975).

Since both noradrenergic and 5-hydroxytryptaminergic systems have been shown to modify dopaminergic mechanisms, we have investigated the ability of clonidine to alter dopamine-dependent behaviours in rodents. Clonidine (range 0.06–2 mg/kg) potentiated circling behaviour induced by both apomorphine (0.25 mg/kg, s.c.) and amphetamine (3 mg/kg, i.p.) in mice with unilateral destruction of the nigro-striatal dopaminergic pathway. Similarly, this dose range of clonidine enhanced apomorphine (2 mg/kg)-induced reversal of reserpine akinesia in mice. The drug also potentiated apomorphine-induced hyperactivity resulting from bilateral injections (10 µg) into the nucleus accumbens of rats. Clonidine (100 µg) into one striatum of rats produced no postural asymmetry or circling behaviour, nor was this pretreatment evoked into active turning activity in the presence of systematically administered apomorphine (0.5 mg/kg, s.c.). Clonidine (0.5 mg/kg, i.p.) was without effect on apomorphine (0.1–5 mg/kg, s.c.)-induced stereotypy in rats, but did enhance the catalepsy induced by haloperidol (0.1–2 mg/kg, i.p.) in rats.

This study suggests that clonidine significantly modifies all dopamine-dependent behaviours exhibiting a motor component, *viz*, circling behaviour and locomotor activity. It failed to apparently influence stereotypy or to directly affect striatal dopaminergic mechanisms. Although clonidine potentiated the cataleptic effect of a neuroleptic, its action is likely to be one of non-specific sedation rather than one of a true synergistic monoaminergic mechanism.

Whatever the mechanism of action of clonidine, be it through a noradrenergic, tryptaminergic or any other neuronal system, it appears that such actions do not influence all forms of dopamine mediated behaviour.

CJP is a Fellow of the Parkinson's Disease Society.

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