Antagonism of apomorphine and lergotrile hypothermia

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There is now considerable evidence to suggest that more than one type of dopamine receptor exists within the central nervous system (Iversen, 1978, Tye, *et al.*, 1977). It has also been reported that apomorphine and the ergot dopamine agonists may act as selective agonists for the different dopamine receptors. Since dopamine agonists have been shown to lower body temperature (Fuxe & Sjoqvist 1972, Cox & Lomax 1977, Cox & Lee 1977) we have examined the hypothesis that different dopamine antagonists may preferentially antagonise the hypothermic response produced by either apomorphine or lergotrile.

Male albino MFI mice (20–30 g) were used in all the experiments. Rectal temperature was measured immediately prior to and every 30 min for 90 min following treatment with apomorphine, lergotrile or saline. In some experiments animals were pretreated with haloperidol, pimozide or the respective vehicle 1 h prior to the start of the experiment.

Apomorphine (5 mg/kg) and lergotrile (5 mg/kg) produced a fall in body temperature of 3.5 to 5°C. Haloperidol (0.4 mg/kg and 1 mg/kg) antagonised the hypothermic response produced by apomorphine (5 mg/kg, $P < 0.01$). Haloperidol (0.5 mg/kg) partially antagonised the hypothermic response produced by lergotrile (5 mg/kg, $P < 0.01$), however higher doses (1 mg/kg and 2 mg/kg s.c.) had no effect. Pimozide (0.5 mg/kg and 1 mg/kg s.c.) antagonised the hypothermic response produced both by apomorphine (5 mg/kg) and lergotrile (5 mg/kg, $P < 0.01$). A higher dose of pimozide (2 mg/kg) partially antagonised the fall in body temperature produced by lergotrile (5 mg/kg s.c., $P < 0.05$), but had no effect on the hypothermic response produced by higher doses. Haloperidol (0.2 mg/kg–1.5 mg/kg s.c.) and pimozide (0.5 and 1 mg/kg) cause a shift to the right of the dose response curve for apomorphine, however a similar effect for lergotrile only occurs when doses of haloperidol (0.5 mg/kg) and pimozide (0.5 mg/kg and 1 mg/kg) are used, higher doses of either neuroleptic having no effect. This work suggests that the hypothermic responses produced by apomorphine and lergotrile are mediated by different mechanisms.

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Specific [^{3}H]-imipramine binding in rat brain

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Tricyclic antidepressants inhibit the neuronal uptake of noradrenaline and serotonin (Glowinski & Axelrod, 1964). In addition they interact directly with muscarinic cholinoceptors (Snyder & Yamamura, 1977), alpha-adrenoceptors (U'Prichard, Greenberg, Sheenan & Snyder, 1978), serotonin (Bennett & Aghajanian, 1975) and histamine (Green & Maayani, 1977) receptors. Which, if any, of these actions are responsible for the primary therapeutic activity of these drugs is unclear. Following the success of receptor binding techniques in opening a new approach to the study of the mechanism of action of benzodiazepines (Squires & Braestrup, 1977; Möhler & Okada, 1977) we decided to investigate the possible existence of specific high affinity binding sites for tricyclic antidepressants. To date studies with [^{3}H]-amitriptyline or [^{3}H]-imipramine have shown only non-specific (Rehavi & Sokolovsky, 1978) or low affinity binding (O'Brien, Spirt & Horst, 1978).

The binding of [^{3}H]-imipramine was measured by incubating washed rat brain membranes at a final