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Effects of atropine and pimozide on hypothermia induced by apomorphine or oxotremorine in rats

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Injection of apomorphine (1.25 to 20 μg) or dopamine (5 to 20 μg) into the preoptic-anterior hypothalamus of the rat caused a dose related fall in body temperature, which was reversed by pretreatment with pimozide (0.5 mg/kg i.p.; Cox & Lee, 1977)

In this study we have tested the specificity of the blockade by pimozide by comparing its effects on apomorphine-induced hypothermia with those on the hypothermia induced by the muscarinic agonist oxotremorine. The ability of atropine to antagonize apomorphine or oxotremorine-induced hypothermia has also been tested.

Two types of experiment were performed. In the first series the effects of unilateral intrahypothalamic injection of apomorphine and oxotremorine were compared in control rats and in rats pretreated systemically with either atropine or pimozide. In the second series the agonists were injected by the systemic route and the antagonists were given by bilateral intrahypothalamic injection. Intrahypothalamic drug injections were made in a dose volume of 1 μl through previously implanted guide cannulae. Core temperature was measured with a rectal thermistor probe at an ambient temperature of 17 ± 1°C.

The hypothermia after intrahypothalamic injection of apomorphine was reversed by systemic pimozide ($P < 0.01$) but unaffected by systemic atropine (Table 1). Conversely intrahypothalamic oxotremorine was significantly antagonized by atropine, but not by pimozide. Similar results were obtained when the routes of injection of agonist and antagonist were reversed.

Table 1 Effect of atropine and pimozide on hypothermia induced by apomorphine or oxotremorine in rats

	Mean change in core temperature (°C ± s.e. mean)			
Drug	*Saline i.p.*	*Pimozide (0.5 mg/kg i.p.)*	*Atropine (0.5 mg/kg i.p.)*	*Atropine (2.5 mg/kg i.p.)*
Apomorphine (10 μg i.h.)	−0.9 ± 0.2	+0.4 ± 0.1**	−0.7 ± 0.2	−0.9 ± 0.2
Oxotremorine (1.25 μg i.h.)	−0.5 ± 0.05	−0.3 ± 0.2	−0.2 ± 0.03*	−0.08 ± 0.06**
	Saline i.h.	*Pimozide (0.5 μg i.h.)*[1]	*Atropine (0.5 μg i.h.)*[1]	*Atropine (2.5 μg i.h.)*[1]
Apomorphine (1.25 mg/kg i.p.)	−1.8 ± 0.2	−0.9 ± 0.2*	−1.4 ± 0.3	−1.5 ± 0.27
Oxotremorine (0.25 mg/kg i.p.)	−3.1 ± 0.3	−2.5 ± 0.1	−1.8 ± 0.3*	−1.3 ± 0.11**

[1] Injection made bilaterally into the hypothalamus (i.h.), n = between 3 and 13 observations, *$P < 0.05$, ** $P < 0.01$ Mann-Whitney U test.

These experiments lead to the following conclusions. First, pimozide blocks apomorphine specifically, probably by acting on dopamine receptors. Second, as atropine was ineffective against apomorphine, it is unlikely that there is a 'cholinergic link' in dopamine receptor mediated hypothermia in the rat, although such a link has been reported in the mouse (Glick & Marsanico, 1974). Finally, the ability of intrahypothalamic injection of antagonists to reduce the response to systemic agonist injection supports the hypothesis that the hypothermia is mediated, at least in part, via receptors within the hypothalamus.

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