The cardiovascular effects of some *N,N*-dialkylated derivatives of 2-amino-5,6-dihydroxy-1,2,3,4-tetrahydronaphthalene after central or peripheral administration in rats

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Members of a series of 2(*N,N*-dialkylated)-5,6-dihydroxy tetrahydronaphthalenes (*N,N*-dialkyl-5,6-diOHATN) (Cannon, Kim, Aleem & Long, 1972), induce presynaptic dopamine-receptor mediated bradycardia during cardioaccelerator nerve stimulation in cats and dogs (Ilhan, Long & Cannon, 1976). In the pithed rat *N,N*-dimethyl-5,6-diOHATN (M7), or *N,N*-diethyl-5,6-diOHATN have been shown to exert potent and selective inhibition of the tachycardia induced by electrical stimulation of the thoracic spinal cord (Hicks & Cannon, 1979), without increasing blood pressure; an effect mediated by presynaptic α-receptors.

The cardiovascular effects of some members of this series of compounds have been examined after central (i.c.v.) or peripheral (i.v.) administration.

Groups of 5–7 female CFE rats (200–300 g) were anaesthetised with urethane (1.25 g/kg; i.p.); blood pressure was measured from a carotid artery, i.v. injections were made via a jugular vein and i.c.v. injections were made according to the methods of Finch & Hicks (1976). In pithed rats, continuous electrical stimulation of the thoracic segment of the spinal cord was performed according to the methods of Drew (1976), at 60 V, 0.3 ms, 0.3 Hz.

Intraventricular administrations of *N,N*-diethyl-5,6-diOHATN; *N,N*-dipropyl-5,6-diOHATN (0.05–1 μg); or M7 (0.5–5 μg), induced dose-related hypotension and bradycardia. Intravenous administration of these compounds (5–20 μg/kg) also elicited hypotension with immediate bradycardia and these i.v.-induced effects were abolished after pithing, while only the bradycardia was significantly ($P < 0.05$) reduced after bilateral vagotomy. The cardiovascular responses, particularly the bradycardia, elicited by submaximal doses of M7 (1 μg, i.c.v.) were antagonised by pretreatment with yohimbine (25–50 μg, i.c.v. 30 min) or prazosin (0.1–10 μg, i.c.v. 30 min). No antagonism of these responses was demonstrated by thymoxamine (50 μg/kg, i.c.v., 30 min) or by pretreatment with either fluphenazine, or haloperidol (1 mg/kg, i.p., 60 min).

In pithed rats cumulative doses of M7, or clonidine (2.5–50 μg/kg, i.v.) inhibited the tachycardia induced by electrical stimulation of the thoracic spinal cord. These peripheral cardioinhibitory effects were antagonised by pretreatment with yohimbine or phentolamine (250 or 500 μg/kg, i.v., 15 min) but not by prazosin (300 μg/kg, i.v., 15 min).

Members of a series of tetrahydronaphthalenes have been shown to possess potent and selective agonist activity in pithed rats at peripheral presynaptic receptors (α_2-effects). The preferential α_2-receptor antagonist yohimbine prevented these cardioinhibitory effects, but prazosin, an α_1-receptor antagonist, had no effect. These same compounds induced marked hypotension and bradycardia after central administration, effects which were antagonised by both prazosin and yohimbine, but not by thymoxamine or dopamine-receptor antagonists.

Thus it would appear that this series of tetrahydronaphthalenes may have differential effects on peripheral and central α-adrenoceptor mechanisms.

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