Cardiovascular responses to centrally administered adrenaline in spontaneous hypertensive rats

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The involvement of central noradrenergic neurones in the control of blood pressure is well established and both clonidine and α-methyldopa are thought to exert their action via these neurones (Finch, 1974; Finch & Haeusler, 1973). The exact role of specific central adrenergic neurones, which have only recently been demonstrated in the rat brain (Hökfelt, Fuxe, Goldstein & Johansson, 1973) in areas known to be involved in the control of blood pressure, however, remains unclear.

Preliminary studies, in various species, have shown that intracerebroventricular (i.c.v.) injections of adrenaline exert a variable effect on blood pressure (Toda, Matsuda & Shimamoto, 1969; Day & Roach, 1974). Intracerebral injections of adrenaline into various regions of the brain also induce centrally mediated changes in blood pressure (Struyker Boudier & Bekers, 1975). The present study sets out to characterize the cardiovascular activity of icv administered adrenaline in spontaneous hypertensive rats.

In conscious spontaneous hypertensive rats, prepared for direct recording of blood pressure by the method of Popovic & Popovic (1960), adrenaline (1–20 μg ICV) in 10 μl of 0.01 N HCl caused a dose-related fall in blood pressure and heart rate, while i.c.v. injections of vehicle were without effect. Pretreatment with phentolamine (100 μg i.c.v.) did not significantly antagonize the hypotension or bradycardia induced by adrenaline (10 μg i.c.v.), while pretreatment with (±)-propranolol (100 μg i.c.v.) completely abolished the bradycardia and reversed the hypotensive effects of adrenaline (10 μg i.c.v.) resulting in an increase in blood pressure. Moreover, the hypotension and bradycardia induced by adrenaline (10 μg i.c.v.) was only slightly reduced by pretreatment with (+)-propranolol (100 μg i.c.v.), while pretreatment with the active isomer (−)-propranolol (100 μg i.c.v.) abolished the bradycardia and reversed the hypotension. Similar antagonism of adrenaline (10 μg i.c.v.) induced responses was obtained after pretreatment with sotalol (100 μg i.c.v.) and with the selective β_1-antagonist metoprolol (100 μg i.c.v.).

These results indicate that i.c.v. administered adrenaline is capable of consistently inducing hypotension and bradycardia in conscious spontaneous hypertensive rats and that, in this hypertensive model at least, these effects are probably mediated by central β-adrenoceptors rather than central α-adrenoceptors.

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Selective blockade of presynaptic tryptamine receptors by (−)-cocaine and (+)-cocaine

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5-Hydroxytryptamine (5-HT) stimulates the rabbit isolated heart by releasing noradrenaline from the terminal sympathetic nerves (Fozard & Mwaluko, 1976). Transmitter release results from activation of specific receptor sites which in terms of potencies of selective agonists are closely similar to the receptors on the cholinergic nerves of the guinea-pig ileum (Fozard & Mobarok Ali, 1976) originally designated 'M' because of their sensitivity to blockade by morphine (Gaddum & Picarelli, 1957). However, morphine is not a selective antagonist of 5-HT on rabbit heart, and therefore a search was instituted for a more selective antagonist and to determine if the responses to 5-HT on both noradrenergic and cholinergic neurones might be similarly affected.