Table 1 Hyperpolarization produced in rat superior cervical ganglia by sympathomimetic amines (a) EC_{50} values (b) antagonism by phentolamine

	a *Agonist* EC_{50} (μM)	*b* *Phentolamine* (10^{-6} M) *dose ratio*
(−)noradrenaline	$1.7 \times 10^{-6} \pm 0.6$ (5)	5.6 ± 0.9 (4)
(±)isoprenaline	$4.1 \times 10^{-6} \pm 0.8$ (6)	157.3 ± 48.1 (4)
(−)phenylephrine	$4.2 \times 10^{-6} \pm 0.4$ (4)	24.7 ± 3.8 (5)
ADTN*	$6.7 \times 10^{-6} \pm 0.4$ (3)	1.3 ± 0.3 (3)
dopamine	$1.7 \times 10^{-5} \pm 0.5$ (4)	2.3 ± 0.1 (4)
(±)amidephrine	$1.1 \times 10^{-3} \pm 3.1$ (3)	

Figures in brackets represent number of experiments.
Values are given as means ± s.e.means.
*2-amino, 6,7-dihydroxytetralin.

Phentolamine (10^{-6} M) produced a variable degree of antagonism, as measured by the dose-ratio (Table 1*b*). Isoprenaline (most sensitive to phentolamine) was resistant to propranolol (10^{-6} M), suggesting the absence of β-receptors. Variations in the effect of phentolamine might reflect (*a*) the presence of dopamine receptors (selectively stimulated by dopamine and ADTN) or (*b*) influence of uptake processes (cf. Langer & Trendelenburg, 1969). The α-receptors might resemble 'presynaptic' α-receptors, in view of the action of clonidine.

M.P.C. is an M.R.C. Student.

References

BROWN, D.A. & MARSH, S. (1974). A very simple method for recording ganglion depolarization. *J. Physiol. Lond.*, **246**, 24–26P.

LANGER, S.Z. & TRENDELENBURG, U. (1969). The effect of a saturable uptake mechanism on the slopes of dose-response curves for sympathomimetic amines and on the shifts of dose-response curves produced by a competitive antagonist. *J. Pharmac. exp. Ther.*, **167**, 117–142.

Do cyclic nucleotides mediate slow postsynaptic potentials in sympathetic ganglia?

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In sympathetic ganglia, it has been proposed that the slow EPSP (excitatory postsynaptic potential) is mediated by cyclic GMP (guanosine 3′,5′-monophosphate) and the slow IPSP (inhibitory postsynaptic potential) by cyclic AMP (adenosine 3′,5′-monophosphate (McAfee & Greengard, 1972). To test this hypothesis we used the sympathetic ganglion of the bullfrog, where the slow PSPs occur in different cell types; the slow EPSP in type B cells and the slow IPSP in type C cells. We applied cyclic GMP and cyclic AMP to determine whether they mimicked the membrane potential and conductance changes involved in the slow postsynaptic potentials. We also used the monobutyryl, dibutyryl, 8-bromo and 8-parachlorophenylthio derivatives of these cyclic nucleotides, which have greater membrane permeability and/or resistance to inactivation by phosphodiesterase. Using the sucrose gap recording technique, no consistent responses to cyclic GMP or its derivatives (1 mM) were observed in 80 tests on 20 preparations. In only 3 preparations was a depolarizing response observed. Additionally, no consistent responses to cyclic AMP or its derivatives (1 mM) were observed in 14 tests on 8 preparations. With intracellular recording from individual B or C cells, responses to the administration of the cyclic nucleotides or their derivatives were also rare, although responses to acetylcholine were observed. The cyclic nucleotides were administered by perfusion, as well as by extracellular or intracellular iontophoresis. In the few cells where responses were observed, there was little correlation between the potential and/or conductance change of the PSP and the response to the cyclic nucleotide. For example, of the 52 B cells tested, 46 had no consistent responses to cyclic GMP or its derivatives. Of the remaining 6 cells,

3 were depolarized and 3 were hyperpolarized, although the slow PSP in this cell type is a depolarizing response. Although synaptic stimulation increases the concentration of both cyclic GMP and cyclic AMP in these sympathetic ganglia (Weight, Petzold & Greengard, 1974), it appears that further investigation is needed to establish a role of these cyclic nucleotides in the mediation of slow postsynaptic potentials.

References

McAFEE, D.A. & GREENGARD, P. (1972). Adenosine 3',5'-monophosphate: electrophysiological evidence for a role in synaptic transmission. *Science* **178**, 310–312.

WEIGHT, F.F., PETZOLD, G. & GREENGARD, P. (1974). Guanosine 3',5'-monophosphate in sympathetic ganglia: increase associated with synaptic transmission. *Science* **186**, 942–944.

Dopamine receptor mediated inhibition by bromocriptine of accelerator nerve stimulation effects in the pithed cat

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It has been postulated by several investigators that adrenergic nerve terminals in various tissues are endowed with dopamine receptors, stimulation of which causes a decrease of transmitter release (Rand, McCullough & Story, 1975; Tayo, 1977). Recently, the new ergopeptine derivative bromocriptine (2-bromo-α-ergocryptine mesylate, Sandoz), which inhibits prolactin secretion (Flückiger, 1972; Del Pozo, Brun Del Re, Varga & Friesen, 1972), has been characterized as a central dopamine receptor agonist (Corrodi, Fuxe, Hökfelt, Lidbrink & Ungerstedt, 1973; Johnson, Loew & Vigouret, 1976). It was therefore of interest to see whether dopamine receptor stimulation with bromocriptine leads to inhibition of peripheral nerve transmission. The present experiments were performed in 59 cats, in which the activation of prejunctional dopamine receptors with apomorphine inhibits the function of postganglionic sympathetic heart nerves (Scholtysik, 1976).

In pithed cats, electrical stimulation of spinal segments C7 and T1 at 0.5 to 32 Hz induced frequency-dependent increases in heart rate due to selective activation of cardiac sympathetic nerves. Bromocriptine (10 μg/kg i.v.) did not affect the resting heart rate but shifted the stimulation frequency-response curve to the right. The inhibition of the stimulation effects was dose-dependent, as was demonstrated by i.v. infusion of bromocriptine (0.5 or 1 μg kg^{-1} min^{-1}) during repeated heart nerve stimulation at 4 Hz. Bromocriptine (10 μg/kg i.v.) inhibited pre- and postganglionic accelerator nerve stimulation effects but failed to modify the dose-response curve to exogenous adrenaline. Therefore, ganglionic blockade or postsynaptic β-adrenoceptor blockade of bromocriptine can be excluded.

In order to investigate the mechanism of this inhibitory action on postganglionic adrenergic neurones of the cat heart, bromocriptine was infused intravenously (1 μg kg^{-1} min^{-1}) following previous injection of either the α-adrenoceptor antagonist phentolamine (1 mg/kg i.v.), the 5-HT antagonist pizotifen (1 mg/kg i.v.), or the dopamine receptor antagonist haloperidol (0.03, 0.1 and 0.3 mg/kg i.v.). Accelerator nerve stimulation at 4 Hz was repeated every 5 minutes. Pretreatment with haloperidol prevented the neuronal inhibitory effect of bromocriptine in a dose-dependent manner. In contrast to haloperidol, phentolamine and pizotifen caused only slight delays in the onset of the inhibitory action of bromocriptine.

These findings suggest that bromocriptine causes postganglionic inhibition of the cardiac adrenergic nerve function, mainly due to stimulation of prejunctional dopamine receptors. The results are compatible with the present concept of the regulation of transmitter release in the adrenergic neurotransmission.

References

CORRODI, H., FUXE, K., HÖKFELT, T., LIDBRINK, P. & UNGERSTEDT, U. (1973). Effects of ergot drugs on central neurons: evidence for a stimulation of central dopamine neurons. *J. Pharm. Pharmac.*, **25**, 409–410.

DEL POZO, E., BRUN DEL RE, R., VARGA, L. & FRIESEN, H. (1972). The inhibition of prolactin secretion in man by CB 154 (2-Br-α-ergokryptine). *J. clin. Endocr. Metabl.*, **35**, 768–771.

FLUCKIGER, E. (1972). Drugs and the control of prolactin secretion. In: *Prolactin and carcinogenesis*, ed. Boyns, A.R. and Griffiths, K., Cardiff: Alpha Omega Alpha Publishing.

JOHNSON, A.M., LOEW, D.M. & VIGOURET, J.M. (1976). Stimulant properties of bromocriptine on central dopamine receptors in comparison to apomorphine, (+)-amphetamine and L-Dopa. *Br. J. Pharmac.*, **56**, 59–68.

RAND, M.J., McCULLOCH, MARION W. & STORY, D.F. (1975). Prejunctional modulation of noradrenergic transmission by noradrenaline, dopamine and acetylcholine. In *Central Action of Drugs in Blood Pressure Regulation*. Eds: Davies, D.S. & Reid, J.P., 94–132. London: Pitman Medical.

SCHOLTYSIK, G. (1976). Dopaminergic inhibition of the function of postganglionic adrenergic heart nerves in cats. *Arch. Pharmacol.*, **293**, Suppl. R2.

TAYO, F.M. (1977). Further evidence for dopaminoceptors in the vas deferens. *Br. J. Pharmac.*, **59**, 511P–512P.