STRUYKER BOUDIER, H.A.J., GIELIEN, W., COOLS, A.R. & ROSSUM, J.M. Van (1974). Pharmacological analysis of dopamine-induced inhibition and excitation of neurones of the snail, *Helix aspersa*. *Arch. Int. Pharmacodyn*, **209**, 324–331.

WOODRUFF, G.N. (1971). Dopamine receptors; a review. *Comp. Gen. Pharmac.*, **2**, 439–455.

WOODRUFF, G.N. & WALKER, R.J. (1969). The effect of dopamine and other compounds on the activity of neurones of *Helix aspersa*; structure-activity relationships. *Int. J. Neuropharmac.*, **8**, 279-289.

Contractile properties of hypertrophied and normal rat hearts

R.A. BROWN & ANNE M. SOLCA

Department of Pharmacology & Biochemistry, Fisons Ltd., Pharmaceutical Division, R. & D. Laboratories, Loughborough, Leics.

Conflicting reports of contractility changes associated with cardiac hypertrophy are found in the literature. An unchanged (Grimm, Kubota & Whitehorn, 1963) reduced (Spann, Buccino, Sonnenblick & Braunwald, 1967) or increased (Kerr, Winterberger & Giambattista, 1961) contractility has been observed. We have compared the performance *in vitro* of hearts from hypertensive and normal rats to establish whether or not cardiac hypertrophy is associated with reduced contractility.

Renal hypertension was induced in male Wistar rats ($n=40$) according to the method of Finch & Leach (1970). A control group ($n=40$) consisted of unilaterally nephrectomized and sham-operated rats. At 5 weeks the mean systolic blood pressures, as measured by the tail cuff technique, were: controls 142.1 ± 4.2 mmHg, hypertensives 226.9 ± 6.0 mmHg (1 mmHg $\simeq$ 133 Pa). Rats were designated 'hypertensive' and included in the study only if their blood pressures were $>$ control + 3 standard deviations. The animals were killed by cervical fracture, the hearts removed and perfused with McEwens (1951) solution at 37°C gassed with O_2/CO_2 (95:5) according to a modified Langendorff technique described by Broadley (1970). Recordings of isometric developed tension were made by the method of Beckett (1970) using a Grass FT03C force-displacement transducer in conjunction with a Devices M19 recorder. The S-A node was destroyed and the hearts paced using bipolar platinum electrodes delivering rectangular pulses of 2.0 ms duration and 2.5 V from a Devices stimulator.

Force-frequency relationships of the 2 groups were examined over heart rates of 270–500 bts/min at a diastolic tension of 2 grams. The relationship between diastolic tension (0.25–20 g) and developed systolic tension was studied in hearts paced at 275 bts/min and the sensitivity of each group to the positive inotropic effects of $CaCl_2$ were studied in hearts paced at 275 bts/min with a diastolic tension of 2 grams. Finally, the hearts were removed from the perfusion apparatus and weighed. Mean dry weights of each group were: controls, 0.189 ± 0.007 g; 'hypertensives' 0.300 ± 0.017 grams. Water content was 81% in each case.

In the above procedures, tension developed by the hypertrophied hearts was less ($P < 0.05$) than controls either per gram diastolic tension, per bt/min or per equivalent dose of $CaCl_2$. However, if in the force-tension experiments diastolic tension was expressed per gram heart weight and developed tensions in the remaining two procedures, expressed as a percentage initial control tension, there was no difference between the performances of the two groups.

To investigate further this apparent relationship between heart weight and contractile performance, the same procedures were repeated using hearts from normal rats ranging in weight from 70 to 550 grams. Dry heart weight range was 0.068 ± 0.003 g to 0.309 ± 0.012 grams. On this basis, the hypertrophied hearts did not show a reduced performance compared with hearts of similar weights derived from normotensive rats.

We conclude that pressure overload induced cardiac hypertrophy in rats need not be associated with reduced contractility, but that the apparently reduced cardiac performance is similar to that of hearts of similar size from normal animals and is related to heart weight.

References

BECKETT, P.R. (1970). The isolated perfused heart preparation: two suggested improvements. *J. Pharm. Pharmac.*, **22**, 818–822.

BROADLEY, K.J. (1970). An analysis of the coronary vascular response to catecholamines using a modified Langendorff heart preparation. *Br. J. Pharmac.*, **40**, (4), 617–629.

FINCH, L. & LEACH, G.D.H. (1970). Contribution of the sympathetic nervous system to the development and maintenance of experimental hypertension in the rat. *Br. J. Pharmac.*, **39**, 317–324.

GRIMM, A.F., KUBOTA, R. & WHITEHORN, W.W. (1963). Properties of myocardium in cardiomegaly. *Circ. Res.*, **12**, 118–124.

KERR, A., WINTERBERGER, A.R. & GIAMBATTISTA, M. (1961). Tension developed by papillary muscles from hypertrophied rat hearts. *Circ. Res.*, **9**, 103–105.

McEWEN, L.M. (1956). The effect on the isolated rabbit heart of vagal stimulation and its modification by cocaine, hexamethonium and ouabain. *J. Physiol.*, **131**, 678–689.

SPANN, J.F., BUCCINO, R.A., SONNENBLINK, E.H. & BRAUNWALD, E. (1967). Contractile state of cardiac muscle obtained from cats with experimentally produced ventricular hypertrophy and heart failure. *Circ. Res.*, **21**, 341–354.

Motor transmission in the vas deferens of guanethidine-treated guinea-pigs

R.C. HENDERSON & M.A. ZAR

Department of Pharmacological Sciences, The Medical School, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 7RU

There are reasons to believe that motor transmission to the longitudinal muscle of guinea-pig vas deferens is non-adrenergic (Ambache & Zar, 1971; Euler & Hedqvist, 1975). Recently, Furness (1974) has advanced fresh evidence against this view. He has found a great reduction in the nerve-mediated contractions of the vas deferens from guanethidine-treated guinea-pigs; the attenuated contractions were restored to normal levels by exposing the isolated preparation first to (+)-amphetamine (DA) and then to noradrenaline (NA). He has interpreted these results to indicate that NA is the motor transmitter in this tissue.

The present experiments were carried out to determine whether or not repletion by exogenous NA of depleted NA stores was an essential pre-requisite for the restoration of nerve mediated responses in the vas deferens.

Vasa from guanethidine-treated guinea-pigs (100 mg/kg, i.p., 24 h earlier) were set up in 10 ml. organ baths in Krebs; contractions on electrical field stimulation (5 pulse-trains, 1 ms, 10 Hz, 12 V, once every min.) were recorded isometrically. The preparations were exposed first to DA, 1 μg/ml for 15 min, then to NA, 0.5 μg/ml for 6 minutes. Twenty minutes after NA-wash-out, DA, 1 μg/ml was re-introduced into the bath. In control contralateral vas, exposure to NA was omitted.

In all experiments ($n=7$) nerve-mediated contractions were virtually completely lost; restoration of the responses, after exposure for 15 min to DA and 6 min to NA was partial ($8.4 \pm 1.7\%$) and substantially lower than in control (NA-untreated) contralateral preparations ($33 \pm 3\%$). Longer exposure to DA (> 90 min) was needed for complete recovery. There was no evidence that treatment with NA facilitated recovery.

In 3 experiments on vasa from guinea-pigs treated 24 h earlier with (−)-β-hydroxyphenethylguanidine (100 mg/kg, i.p.), a more potent agent than guanethidine in depleting NA stores (Fielden & Green, 1967), motor transmission persisted unimpaired.

Histochemical examination of the vasa from guanethidine or (−)-β-hydroxyphenethylguanidine-treated animals showed a total lack of catecholamine fluorescence. Catecholamine fluorescence was missing in vasa from guanethidine-treated animals even after complete recovery of motor transmission on prolonged exposure to DA.

These findings do not lend support to Furness's conclusion (1974) that the reversal of guanethidine-induced block of motor transmission in the vas deferens was dependent upon the repletion of NA-stores and therefore the transmission was adrenergic. The lack of correlation between NA-depletion and motor blockade is consistent with the non-adrenergic nature of motor transmission in this organ.

We thank Dr R. Fielden, Smith Kline & French Ltd for the gift of (−)-β-hydroxyphenethylguanidine.

References

AMBACHE, N. & ZAR, M.A. (1971). Evidence against adrenergic motor transmission in guinea-pig vas deferens. *J. Physiol.*, **216**, 359–389.

EULER, U.S.v. & HEDQVIST, P. (1975). Evidence for α- and β-2-receptor mediated inhibition of the twitch response in the guinea-pig vas deferens by noradrenaline. *Acta physiol. Scand.*, **93**, 572–573.

FIELDEN, R. & GREEN, A.L. (1967). A comparative study of the noradrenaline-depleting and sympathetic-blocking actions of guanethidine and (−)-β-hydroxyphenethyl-guanidine. *Br. J. Pharmac.*, **30**, 155–165.

FURNESS, J.B. (1974). Transmission to the longitudinal muscle of the guinea-pig vas deferens: the effect of pretreatment with guanethidine. *Br. J. Pharmac.*, **50**, 63–68.