

References

FARMER, J.B., KENNEDY, I., LEVY, G.P. & MARSHALL, R.J. (1972). Pharmacology of AH 5158; a drug which blocks both α and β adrenoceptors. *Br. J. Pharmac.*, **45**, 660-675.

KENNEDY, I. & LEVY, G.P. (1975). Combined α and β adrenoceptor blocking drug AH 5158: further studies on α adrenoceptor blockade in anaesthetized animals. *Br. J. Pharmac.*, **53**, 585-592.

LANGER, S.Z. (1974). Presynaptic regulation of catecholamine release. *Biochem. Pharmac.*, **23**, 1793-1800.

The sympathetic nervous system and renovascular hypertension in the rat

H.J. DARGIE*, S.S. FRANKLIN & J.L. REID

Department of Clinical Pharmacology, Royal Postgraduate Medical School, University of London

The integrity of central noradrenergic neurones is essential for the development and maintenance of DOCA salt hypertension in the rat (Haeusler, Finch & Thoenen, 1972; Dargie, Dollery & Lewis, 1975) and perinephritis hypertension in the rabbit (Chalmers, Dollery, Lewis & Reid, 1974). Plasma noradrenaline levels are increased in the DOCA salt model and the rise in both blood pressure and plasma noradrenaline can be prevented by pre-treatment with intracisternal (i.c.) 6-hydroxydopamine (6-OHDA) (Dargie, Lewis, Reid & Zivin, 1975).

We have measured plasma noradrenaline (NA) as an index of peripheral sympathetic activity in a renovascular model of experimental hypertension in the rat and have assessed the relationship between central and peripheral sympathetic activity in the development of hypertension in this model.

Male Wistar rats (weighing 200 g) had a silver clip 0.007 in. wide placed over the left renal artery followed by contralateral nephrectomy. Control rats underwent a sham procedure involving placement of a broad non-constricting clip over the renal artery and contralateral nephrectomy. Blood pressure was measured by tail plethymography at 24 h, 7, 14 and 28 days respectively. The animals were killed by decapitation and the first 1 ml of arterial blood from the trunk was collected in iced heparin tubes for estimation of NA by the method of Henry, Starman, Johnson & Williams (1975).

Two groups of rats were pre-treated 14 days before with intracisternal 6-OHDA or ascorbate saline vehicle. Renal arterial clip or sham operations were carried out on each group. Blood pressure was measured after 7 days, the animals were decapitated and blood collected.

In the first series of experiments blood pressure

was significantly elevated ($P < 0.01$) in the rats with renal arterial clips at 24 h, 7, 14 and 28 days. Mean systolic blood pressure (\pm s.e. mean) ranged from 144 ± 5 mmHg at 24 h to a maximum of 177 ± 9 at 14 days. Blood pressures (in corresponding 'sham-operated' rats) were 109 ± 4 and 115 ± 4 mmHg. Plasma NA in the clip groups was higher than sham operated rats at each time examined. These differences were significant at 7, 14 and 28 days. At 14 days plasma NA was 1.91 ± 0.32 μ g/ml in clip groups and 0.93 ± 0.24 ng/ml in sham operated controls ($P < 0.05$).

Blood pressure and plasma noradrenaline were elevated in the group of rats given i.c. vehicle and renal arterial clip. However, in the group pretreated with i.c. 6-OHDA blood pressure and plasma noradrenaline levels did not rise and were not significantly different from their controls.

It is concluded that peripheral sympathetic activity is increased in the one kidney Goldblatt model of experimental hypertension and that this increase in sympathetic activity is mediated by catecholamine mechanisms in the central nervous system.

References

CHALMERS, J.P., DOLLERY, C.T., LEWIS, P.J. & REID, J.L. (1974). The importance of central adrenergic neurones in renal hypertension in rabbits. *J. Physiol., Lond.*, **238**, 403-411.

DARGIE, H.J., DOLLERY, C.T. & LEWIS, P.J. (1975). Role of saline consumption in the prevention of DOCA salt hypertension by central 6-hydroxydopamine; role of saline intake. *Br. J. Pharmac.*, **53**, 455P.

DARGIE, H.J., LEWIS, P.J., REID, J.L. & ZIVIN, J.A. (1975). Mechanism of the prevention of DOCA saline hypertension by central 6-hydroxydopamine. *Proceedings 6th International Congress of Pharmacology, Helsinki, Finland* (in press).

HAESLER, G., FINCH, L. & THOENEN, H. (1972). Central adrenergic neurones and the initiation and development of experimental hypertension. *Experientia*, **28**, 1200-1203.

HENRY, D.P., STARMAN, B.J., JOHNSON, D.G. & WILLIAMS, K.N. (1975). A sensitive radioenzymatic assay for norepinephrine in tissues and plasma. *Life Sci.*, **16**, 375-384.