during the oestrous cycle, the changes running parallel in the four brain regions, the ovaries and the adrenal glands. The highest values were observed on the days of pro-oestrus and di-oestrus and the lowest 3 h after onset of red light on the day of oestrus. A very low uterine monoamine oxidase activity during oestrus and a very high uterine monoamine oxidase activity during met-oestrus coincided with low ovarian progesterone secretion rates during oestrus and high secretion rates during met-oestrus (Hashimoto, Henricks, Anderson & Melampy, 1968; Fajer, Holzbauer & Newport, 1971). Similarly, the monoamine oxidase activity in human endometrium was found to be increased during periods of increased progesterone concentrations in the blood (Southgate, Grant, Pollard, Pryse-Davies & Sandler, 1968). A rise in monoamine oxidase activity during increased locomotor activity was most pronounced on the day of met-oestrus. In contrast, on the day of oestrus monoamine oxidase activity was lowest when the rats became active.

The monoamine oxidase activity in the septum of castrated male rats was about double that in castrated female rats.

The increase in monoamine oxidase activity of the rat heart after adrenalectomy described by Avakian & Callingham (1968) was confirmed. In addition, there was a rise in the monoamine oxidase activity of the hypothalamus by 45%.

The interrelation between steroid hormones and brain monoamine oxidase may be linked with the depressant effect of certain steroids on the central nervous system (Gyermek, Genther & Fleming, 1967). Brain amines are also thought to be involved in the chain of events which lead to the release of pituitary hormones. Steroids might exert their feed-back mechanism on the brain by affecting brain amine metabolism.

M.B.H.Y. is grateful to the Wellcome Trust for the support of this work.

REFERENCES

- AVAKIAN, V. M. & CALLINGHAM, B. A. (1968). An effect of adrenalectomy upon catecholamine metabolism. Br. J. Pharmac. Chemother., 33, 211P.
 FAJER, A. B., HOLZBAUER, M. & NEWPORT, H. M. (1971). The contribution of the adrenal gland
- to the total amount of progesterone produced in the female rat. J. Physiol., Lond., 214, 115-126.
- GYERMEK, L., GENTHER, G. & FLEMING, N. (1967). Some effects of progesterone and related steroids on the central nervous system. Int. J. Neurochem., 6, 191–198. HASHIMOTO, I., HENRICKS, D. M., ANDERSON, L. L. & MELAMPY, R. M. (1968). Progesterone and
- pregn-4-en-20a-ol-3-one in ovarian venous blood during various reproductive states in the rat.
- Endocrinology, 82, 333-341. SOUTHGATE, J., GRANT, E. C. C., POLLARD, W., PRYSE-DAVIES, J. & SANDLER, M. (1968). Cyclical variations in endometrial monoamine oxidase: correlation of histochemical and quantitative biochemical assays. Biochem. Pharmac., 17, 721-726.

Failure to induce experimental hypertension in rats after intraventricular injection of 6-hydroxydopamine

L. FINCH, G. HAEUSLER* and H. THOENEN

Department of Experimental Medicine, F. Hoffman-La Roche & Co. Ltd., Basle, Switzerland

Injections of 6-hydroxydopamine into a lateral brain ventricle of rats produce a marked and long-lasting depletion of brain catecholamines (Uretsky & Iversen, 1970). A possible relationship between the activity of central adrenergic neurones and the development of deoxycorticosterone-(DOCA) sodium chloride hypertension in rats (Nakamura, Gerold & Thoenen, 1971), and of neurogenic hypertension in rabbits (Chalmers & Wurtman, 1971), has been proposed. The current study was undertaken to obtain further information on the possible role of central adrenergic neurones in the regulation of blood pressure, and on their importance in various forms of experimental hypertension.

Intraventricular injection of 6-hydroxydopamine $(3 \times 250 \ \mu g)$ lowered the blood pressure of 12 week old normotensive (mean blood pressure 125 mmHg) and spontaneously hypertensive (Japanese strain) rats (mean blood pressure 195 mmHg) by approximately 10 mmHg and 40 mmHg, respectively. This effect was transient and disappeared after 4-5 days (Haeusler, Gerold & Thoenen, 1970). A similar treatment of DOCA-sodium chloride (mean blood pressure 213 mmHg) and renal hypertensive rats (mean blood pressure 218 mmHg) had no significant effect on the blood pressure. The noradrenaline content of the hypothalamus, the medulla oblongata and the remaining parts of the brain was lowered to 19, 56 and 15%, respectively, of that of vehicle injected controls; the tyrosine hydroxylase activity was reduced to 45, 54 and 15%, respectively. Thus, in spite of an extensive destruction of central adrenergic structures the blood pressure of normotensive and spontaneously hypertensive rats was only slightly reduced and that of DOCA-sodium chloride and renal hypertensive rats was not affected at all.

If, however, the intraventricular injections of 6-hydroxydopamine were given 7-10 days before the induction of DOCA-sodium chloride or renal hypertension, their development was completely prevented. Similarly, 6-hydroxydopamine injected into the lateral ventricle of 7 week old spontaneously hypertensive rats (mean blood pressure 165 mmHg) lowered the blood pressure to 150 mmHg. The blood pressure remained at this value during the next 5 weeks whilst, in vehicle injected spontaneously hypertensive rats, it rose to approximately 200 mmHg.

It is concluded that intraventricular injection of 6-hydroxydopamine prevents the development of various forms of experimental hypertension, but is ineffective in established hypertension. This effect of 6-hydroxydopamine is probably due to the destruction of central noradrenergic and/or dopaminergic structures which are involved in the initiation of hypertension, but which seem to be of no importance for the maintenance of established hypertension. No information can be given as to the localization of these structures within the central nervous system.

REFERENCES

- CHALMERS, J. P. & WURTMAN, R. J. (1971). Participation of central noradrenergic neurons in arterial baroreceptor reflexes in the rabbit. *Circulation Res.*, 28, 480-491.
- HAEUSLER, G., GEROLD, M. & THOENEN, H. (1970). Blood pressure and heart rate of normotensive and hypertensive rats after injection of 6-hydroxydopamine into a lateral ventricle. Naunyn-Schmiedebergs Arch. exp. Path. Pharmak., 266, 345-346. NAKAMURA, K., GEROLD, M. & THOENEN, H. (1971). Experimental hypertension of the rat: Reci-
- procal changes of norepinephrine turnover in heart and brain-stem. Naunyn-Schmiedebergs Arch. exp. Path., Pharmak., 268, 125-139.
 URETSKY, N. J. & IVERSEN, L. L. (1970). Effects of 6-hydroxydopamine on catecholamine containing

neurones in the rat brain. J. Neurochem., 17, 269-278.

The recovery of vascular adrenergic nerve function in the rat after chemical sympathectomy with 6-hydroxydopamine

L. FINCH*, G. HAEUSLER, H. KUHN and H. THOENEN

Department of Experimental Medicine of F. Hoffmann-La Roche & Co. Ltd., Basle, Switzerland

Morphological and biochemical studies have demonstrated that 6-hydroxydopamine causes a selective destruction of adrenergic nerve terminals in both the rat and cat