taken 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 (3×250 μg) 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.

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

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

(Thoenen & Tranzer, 1968). The nerve terminals regenerate after 6-hydroxydopamine, and in the cat the return of normal responses to sympathetic nerve stimulation occurs 4 weeks after the initial dose of 6-hydroxydopamine (Haeusler, Haefely & Thoenen, 1969). Conflicting results have been published on the role of the sympathetic nervous system for the development of hypertension. While immunosympathectomy prevented the induction of genetic hypertension (Clark, 1971), previous chemical sympathectomy with 6-hydroxydopamine had no effect on the development of deoxycorticosterone-sodium chloride and renal hypertension (Clarke, Smookler & Barry, 1970; Finch & Leach, 1970). In the present work the recovery of adrenergic nerve function in the vascular system was studied in more detail.

6-Hydroxydopamine hydrobromide was injected intravenously on day 1 (2×50 mg/kg) and on day 7 (2×100 mg/kg). On day 8 the pressor responses to stimulation of the entire sympathetic outflow in pithed rat preparations (Gillespie & Muir, 1967) were completely abolished. These animals had previously been adrenalectomized and treated with corticosterone (5 mg/kg, i.m.). A 50% recovery of the pressor responses was observed between day 10 and 14 and a virtually complete recovery by day 28. The pressor responses to tyramine in pithed rats and to physostigmine in urethane anaesthetized rats were also abolished on day 8, but by day 14 they were virtually identical with those of control rats. A similar rapid recovery of the effect of perivarterial nerve stimulation was observed in isolated perfused renal artery preparations. The sensitivity of this preparation to exogenous noradrenaline was not influenced by 6-hydroxydopamine. In rats anaesthetized with pentobarbitone, contractions of the lower eyelids were measured during stimulation of the cervical sympathetic trunk. These contractions were completely abolished on day 8, showed a moderate recovery between day 14 and day 21, and returned to normal by day 28.

The determination of noradrenaline content in the hearts, salivary glands, renal and mesenteric arteries revealed, on day 8, a depletion by 6-hydroxydopamine to 5, 9, 33 and 40%, respectively, of that of controls with a subsequent gradual rise in all organs. In electronmicrographs of mesenteric arterioles destruction of adrenergic nerve endings by 6-hydroxydopamine seemed to be virtually complete.

The results point to a very rapid restoration of adrenergic nerve function after 6-hydroxydopamine in blood vessels and thus could explain the failure of 6-hydroxydopamine to prevent the development of experimental hypertension.

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