

# INHIBITION OF THE BLOOD PRESSURE RESPONSE TO $\alpha$ -METHYLDOPA IN UNANESTHETIZED RENAL HYPERTENSIVE RATS BY NEONATAL 6-HYDROXYDOPAMINE (6-OHDA) TREATMENT

WYBREN DE JONG, ABRAHAM P. PROVOOST and FRANS P. NIJKAMP  
Rudolf Magnus Institute for Pharmacology, Medical Faculty,  
University of Utrecht, Utrecht, The Netherlands

NEONATAL treatment with 6-hydroxydopamine (6-OHDA), given subcutaneously in a dose of 100  $\mu\text{g/g}$  on day 1 and 2 and of 250  $\mu\text{g/g}$  on day 8 and 15, caused a permanent depletion (88–99 per cent) of noradrenaline (NA) in heart, spleen and kidneys, but not in adrenals. At 26 weeks of age no evidence of regeneration of NA levels was observed (PROVOOST, DE KEMP and DE JONG, 1973). Effectiveness of this treatment was also indicated by increased sensitivity to the NA pressor response. In 10–12-week-old rats anesthetized with pentobarbital there was a five-fold increased sensitivity to various doses of intravenously (i.v.) administered NA. In contrast, the pressor response to i.v. administered tyramine was greatly diminished. In the pithed and adrenalectomized 6-OHDA-treated rat only minimal pressor responses were obtained by electrical stimulation (supramaximal voltage) of the sympathetic outflow of the spinal cord; i.e. less than 5 per cent of the value obtained in controls. These data probably indicate that a high degree of functional sympathetic denervation was achieved by the administration of 6-OHDA to the new-born rat.

This treatment failed to prevent the development of renal hypertension induced in 6-week-old rats by application of a solid silver clip (LEENEN and DE JONG, 1971)

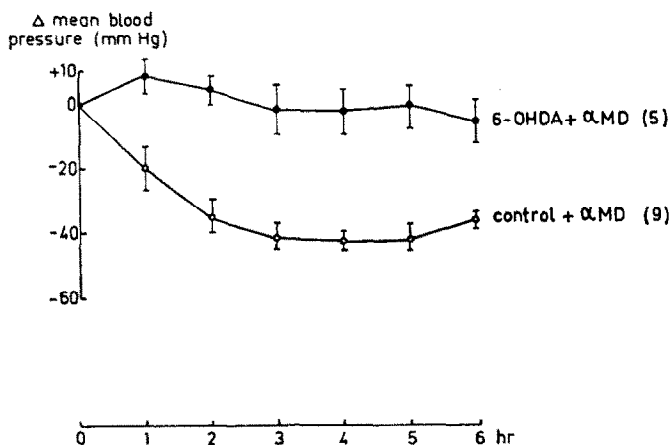


FIG. 1.—Effect of i.p.  $\alpha$ -methyl dopa ( $\alpha$ MD, 200 mg/kg) on mean blood pressure of unanesthetized renal hypertensive rats. Animals had been treated after birth with 6-hydroxydopamine (6-OHDA, ●—●) or vehicle (control, ○—○). The number of rats used is indicated in parentheses, means  $\pm$  S.E.M. are given.

(internal diameter 0.20 mm) on one renal artery. Blood pressure measurements in unanesthetized rats were done by means of an indwelling chronic iliac cannula. Four weeks after surgery the blood pressure level reached was as high in 6-OHDA-treated renal hypertensive rats as in those treated with vehicle only after birth. Presumably the catecholamines released from the adrenal medulla have an important role in maintaining hypertension in the 6-OHDA-treated rats. The effect of  $\alpha$ -methyldopa ( $\alpha$ -MD; 200 mg/kg intraperitoneal (i.p.)) was examined in both groups of hypertensive rats, since previous studies (HENNING, 1969; DAY, ROACH and WHITING, 1973 and NIJKAMP and DE JONG, unpublished data) indicated that in the unanesthetized renal hypertensive rat the decrease in blood pressure induced by  $\alpha$ -MD totally depends on the central action of this drug. As shown in Fig. 1 the decrease in blood pressure after  $\alpha$ -MD was virtually absent in the rats treated with 6-OHDA neonatally, while a decrease of  $43 \pm 3$  mm Hg was found in controls.

These preliminary data are interpreted as indicating a role of inhibition of sympathetic nervous function in the blood pressure decrease induced by  $\alpha$ -MD in the awake renal hypertensive rat.

#### REFERENCES

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