Short communications

Aortic reactivity and electrophysiology in normotensive rats, spontaneously hypertensive rats and rats made hypertensive with desoxycorticosterone plus salt

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The mechanical and electrophysiological activity of rings and strips of thoracic aortic smooth muscle taken from normotensive, DOCA-hypertensive and New Zealand spontaneously hypertensive (A.S. strain) rats have been compared. Aortae from A.S.-hypertensive rats developed less tension in the presence of noradrenaline and K^+ than those isolated from normotensive and DOCA-hypertensive rats. Aortae from DOCA-hypertensive rats developed the same tension in response to K^+ as normotensive rats but were less reactive to noradrenaline. Measurements of resting membrane potentials from the three groups of rats demonstrated that whereas normotensive and DOCA-hypertensive rats had similar resting membrane potentials, those from A.S.-hypertensive rats were significantly lower ($P<0.001$). It is suggested that the enhanced responsiveness of intact vascular beds in A.S.-hypertensive rats is a consequence of a change in the geometry of the blood vessels rather than an increase in the contractor response of the smooth muscle cells.

Pickering (1955) concluded that arterial pressure behaved like a graded characteristic so far as inheritance was concerned, with hypertensives constituting the right-hand tail of a normal distribution curve. Clearly, the New Zealand strain of rats with genetical hypertension offered an opportunity to study the pathogenesis of a spontaneously occurring hypertension which might well have analogies with essential hypertension in man.

Initially, Laverty & Smirk (1961) reported that rats with genetical hypertension had an increased innervated hind limb resistance and suggested that the increased resistance was neurogenic in origin. Subsequently it was realized that blood vessels of the hind limb and mesenteric vascular beds in genetically hypertensive rats reacted more strongly to vasoconstrictor substances (Laverty, McGregor & McQueen, 1968). Since this could either be the result of an increase in the reactivity of the vascular smooth muscle or a change in the geometry of the blood vessels, that is an increase in the wall thickness to lumen diameter ratio, it was decided to compare the reactivity of aortic rings and electrophysiology of aortic strips obtained from normotensive rats with those taken from New Zealand spontaneously hypertensive (A.S. strain) rats and rats made hypertensive with desoxycorticosterone (DOCA) plus salt.

Methods.—Female rats only were used in this study and weighed approximately 200–300 g.

(i) *Mechanical studies*

Thoracic aortic rings approximately 3 mm in length were set up in 3 ml gut baths under a resting tension of 1 g and bathed with a modified Krebs solution (NaCl, 133; $NaHCO_3$, 25; KCl, 4·5; $MgSO_4$, 1·25; $CaCl_2$, 2·5; dextrose, 10; and $CaNa_2$ EDTA, 0·026 mM) aerated with 95% O_2, 5% CO_2. Experiments were conducted at 32° C after allowing the tissues to equilibrate for 1·5 hours. Cumulative dose-response curves were obtained to L-noradrenaline bitartrate (1–50 ng/ml) and after a recovery period, to K^+ by replacement of the Na^+ in the modified Krebs.

(ii) *Electrophysiological studies*

Spirally cut strips of aortae 1 cm long were mounted horizontally in a Perspex bath through which the aerated modified Krebs solution flowed continuously at 4 ml/minute. Similar initial tensions and equilibration times as in the mechanical studies were used in this series of experiments.

Transmembrane potentials were measured with glass microelectrodes filled with 3M KCl. The electrodes had resistances between 20 and 50 MΩ and tip diameters of approximately 0·2 μm.

Results.—Rat blood pressures (1 mmHg ≡1·333 mbar) were measured by the tail-cuff method (Lessin, 1965) on at least 2 separate days before the experiment.

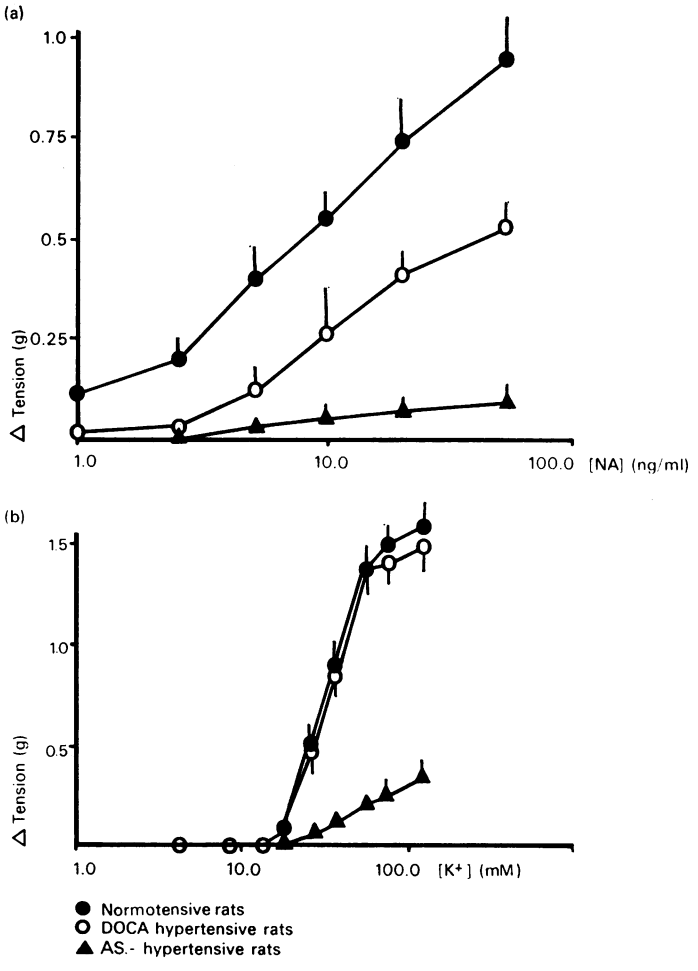

FIG. 1. (a) Dose-response relationship to noradrenaline of aortic rings from normotensive ($n=8$); DOCA-hypertensive ($n=7$) and A.S.-hypertensive rats ($n=10$). Values are means ±S.E. (b) Dose-response relationship to K^+ of aortic rings from normotensive ($n=22$); DOCA-hypertensive ($n=11$) and A.S.-hypertensive rats ($n=16$). Values are means ± S.E.

The normotensive group of seventeen animals had a mean systolic blood pressure of 140·5±1·9 (±S.E. of mean) and a body weight of 204·8±5·8 (±S.E.M.). The DOCA-hypertensive and A.S.-hypertensive groups, each consisting of ten animals, had mean systolic blood pressures of 211·1±6·9 and 221·8±6·9, respectively, and body weights of 248·3±8·0 and 202·1±4·1, respectively.

In every experiment the reactivity of aortae from A.S.-hypertensive rats to noradrenaline and K^+ was markedly reduced whereas the reactivity of aortae from rats with DOCA-hypertension was unchanged to K^+ and about 40% reduced to noradrenaline (Fig. 1a, b).

Measurement of resting membrane potentials of aortic smooth muscle cells demonstrated that the normotensive animals had a mean resting membrane potential of 23·97±0·45 mV (±S.E.M.).

The mean of the DOCA group was not significantly different from the normotensives, being 24·47±0·33 mV, but that from the A.S.-hypertensive rats was 16·08±0·31 mV which is significantly lower ($P>0·001$) than the other two groups. The number of cells penetrated during the measurement of these potentials was 250 from the

normotensive group and 120 in each of the hypertensive groups.

Discussion.—Although the resting membrane potentials obtained from the aortae were lower than those reported for other vascular smooth muscle, confidence in these values was strengthened by the finding that resting membrane potentials of approximately 60 mV were recorded from rat portal vein preparations. These values are similar to those reported by Funaki & Bohr (1964).

The results suggest that the enhanced responsiveness of intact vascular beds in A.S.-hypertensive rats is a consequence of a change in the geometry of the blood vessels rather than an increase in the contractor response of the smooth muscle cells.

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