

# matters arising

## Sympathoadrenal medullary activity in young, spontaneously hypertensive rats

INCREASED levels of serum dopamine- $\beta$ -hydroxylase (DBH) have been reported in spontaneously hypertensive rats (SHRs)<sup>1</sup>. Although DBH is released from sympathetic nerve endings along with noradrenaline, levels of the enzyme in plasma do not seem to reflect accurately the degree of sympathoadrenal activity<sup>2</sup>. Plasma levels of noradrenaline mostly reflect sympathetic neuronal activity whence adrenaline (A) levels are indicative of adrenal medullary discharge. The content of catecholamines and biosynthetic

were derived were used as controls. Activities of adrenal tyrosine hydroxylase (TH), DBH, and phenylethanolamine-N-methyl transferase (PNMT), as well as plasma DBH, were also examined.

Male rats, 4 weeks old and weighing 70–90 g, were decapitated, and the first 1.5 ml of blood, which was ejected in a pulsatile stream from the trunk, was collected in heparinised tubes kept on ice. After centrifugation at 6,000g for 20 min at 4 °C, an aliquot of the plasma was removed for an assay of the DBH activity<sup>3</sup>. The proteins in 400  $\mu$ l of the plasma were precipitated by the addition of 10  $\mu$ l of 40% perchloric acid, and the mixture was kept at –10 °C until it was assayed for total catecholamines (adrenaline + noradrenaline)<sup>5</sup> and noradrenaline<sup>6,7</sup>.

TH, DBH, and PNMT in the adrenals of 4-week-old SHR were decreased (Table 2). Furthermore, the A content of the adrenals of the SHRs were lower than those of the WKY.

These observations are consistent with the view that, at 4 weeks of age, sympathetic neuronal activity in SHRs is increased, whereas adrenal medullary activity is depressed. Adrenal medullary activity is increased when sympathetic nerves are destroyed by 6-hydroxydopamine<sup>12</sup> and it is likely that depressed adrenal medullary activity may be secondary to the increased sympathetic neuronal activity. The exaggerated sympathetic neuronal activity at that age may be an essential factor in the course of development of hypertension in SHRs.

During this study, H.G. was supported by the Deutsche Forschungsgemeinschaft, Bonn, West Germany. J.M.S. is a visiting scientist at the National Institute of Mental Health, and M.F.R. is a research associate in the Pharmacology-Toxicology Program of the National Institute of General Medical Sciences.

**Table 1** Catecholamine concentrations\* and dopamine- $\beta$ -hydroxylase activity\* in the plasma of 4-week-old spontaneously hypertensive and normal rats

	WKY	SHR
Total catecholamines	11.9 $\pm$ 0.07	13.2 $\pm$ 0.8
Noradrenaline	1.8 $\pm$ 0.14	2.93 $\pm$ 0.35†
Dopamine- $\beta$ -hydroxylase	7.84 $\pm$ 0.24	13.4 $\pm$ 0.6†

\* Results expressed as ng of catecholamines, ng of noradrenaline and units of enzyme per ml of plasma, and are the means ( $\pm$  s.e.m.) for groups of 14 animals.

†  $P < 0.001$  compared with control animals.

‡  $P < 0.01$  compared with control animals.

**Table 2** Catecholamine content\* and biosynthetic enzyme activities\* in the adrenal glands of 4-week-old spontaneously hypertensive and normal rats

	WKY	SHR
Tyrosine hydroxylase	11.9 $\pm$ 0.48	8.67 $\pm$ 0.24†
Dopamine- $\beta$ -hydroxylase	25.6 $\pm$ 2.6	17.7 $\pm$ 0.92†
Phenylethanolamine-N-methyl transferase	8.43 $\pm$ 0.18	5.13 $\pm$ 0.12†
Adrenaline	2.15 $\pm$ 0.15	1.70 $\pm$ 0.09§
Noradrenaline	0.85 $\pm$ 0.10	0.75 $\pm$ 0.04

\* Results are expressed as ng of catecholamines, ng of noradrenaline, and units of enzyme per mg of adrenal and are the mean values ( $\pm$  s.e.m.) for groups of 14 animals.

†  $P < 0.001$  compared with control animals.

‡  $P < 0.01$  compared with control animals.

§  $0.02 < P < 0.05$ .

enzymes in the adrenal are presumably indices of the activity of the adrenal medulla in synthesising and releasing catecholamines. The possible role of the sympathoadrenal system in initiating the increase in blood pressure in SHRs was examined by measuring levels of adrenaline and noradrenaline in the plasma and adrenal glands at the age of 4 weeks, the age at which the blood pressure of SHR begins to rise<sup>8</sup>. Normotensive rats of the Wistar Kyoto strain (WKY) from which the SHRs

The catecholamine content of the adrenals was assayed fluorimetrically<sup>8</sup>, and the TH (ref. 9), DBN (ref. 4), and PNMT (ref. 10), activities were assayed radiometrically.

In young SHRs the plasma levels of both the noradrenaline and the DBH were increased over those of the WKY (Table 1) but the total catecholamines (mostly A) were not significantly different. In contrast to the increased TH and DBH activities in the adrenal glands of adult SHR<sup>11</sup>, the activities of

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NAGATSU REPLIES—The findings of Grobecker *et al.*<sup>1</sup> agree with previous results<sup>2</sup> on increased serum DBH of SHRs at 3 weeks of age, and are consistent with the view that sympathetic neuronal activity in young SHRs is increased. As additional evidence, I have found that DBH activity in the mesenteric vessels of SHR at 3 weeks of age is