Dopamine Receptors and β -Adrenergic Receptors Mediating Relaxation in Isolated Renal Arteries from Stroke-Prone Spontaneously Hypertensive Rats. Yoshitaka Nishimura, Yujing Gao, Aritomo Suzuki and Kana Maeda. Department of Pharmacology, Kinki University School of Medicine, Osaka-fu 589.

We have previously reported that dopamine (DA) relaxed rat intrarenal arteries through activation of DA₁ receptors, and that the DA-induced relaxation in intrarenal arteries was larger in stroke-prone spontaneously hypertensive rats (SHRSP) at 6 months of age than in age-matched Wistar-Kyoto rats (WKY) (Clin. Exp. Pharmacol. Physiol. Suppl. 1, 1995). To further elucidate the characteristics of the DA-induced relaxation in the renal arteries from SHRSP, we examined the effects of DA, isoproterenol (ISO), a β -adrenergic receptor agonist, and cyclic AMP-related compounds in the main and intrarenal arteries from WKY and SHRSP at different ages.

Method: Male WKY and SHRSP were used. The systolic blood pressure (mmHg) in WKY and SHRSP were measured by the tail cuff method; they were 131 ± 2 and 162 ± 3 at 1.5 months of age, 136 ± 3 and 210 ± 3 at 3 months of age, and 144 ± 2 and 262 ± 5 at 6 months of age, respectively. Under pentobarbital anesthesia (50mg/kg, i.p.), the rats were exsanguinated from the abdominal aorta, and then the main renal artery and intrarenal artery (third branches of the renal artery) were isolated. The arteries were cut into rings, 1-2 mm in length, and were mounted on two metal holders in an organ chamber filled with Krebs-Henseleit solution maintained at 37°C and aerated with a mixture of 95% O₂ and 5% CO₂. Isometric tension was measured with a force displacement transducer connected to a polygraph. The resting tension in the main renal and intrarenal arteries was adjusted to 1g and 0.2g, respectively. The relaxant effects of drugs were assessed by arteries precontracted with KCl (EC₅₀). For the relaxation study of DA and ISO, the preparations were pretreated with 2 μ M phenoxybenzamine for 60 min to block α -adrenergic receptors irreversibly. The relaxant response to each drug was expressed as a percentage of the maximal relaxation generated by the application of papaverine (100 μ M).

Results and Discussion: DA (0.1-30 μ M) slightly relaxed the main renal arteries from WKY and SHRSP at 1.5 months of age, and the relaxant response did not differ between the two groups. The DA-induced relaxation was not found in the main renal arteries from WKY and SHRSP at 3 and 6 months of age. In the intrarenal arteries, DA produced a potent relaxation in WKY and SHRSP, and the DA-induced relaxation was significantly higher in SHRSP than in age-matched WKY at all ages tested. The DA-induced relaxation in intrarenal arteries attenuated with increasing age in WKY and SHRSP, and the degree of attenuation was greater in WKY than in SHRSP. The relaxation produced by ISO in the main and intrarenal arteries in both groups also declined as the age of the animal increased. The ISO-induced relaxation in main renal arteries was significantly smaller in SHRSP at 3 and 6 months of age than in age-matched WKY, whereas the relaxation in the intrarenal arteries did not differ between the two groups at any age tested. There were no significant differences in the relaxation response to forskolin, dibutyryl cyclic AMP and 3-isobutyl-1-methylxanthine between SHRSP and age-matched WKY in the main and intrarenal arteries at any age tested. In addition, the responses to these agents in the main and intrarenal arteries were not altered with advancing age in either group.

In conclusion, the vasorelaxation mediated by DA₁-receptors and β -adrenergic receptors which are linked to adenylate cyclase are an age-dependent decrease in the rat renal arteries. In addition, SHRSP exhibited the increased DA₁-receptor-mediated response in intrarenal arteries in an early stage of the development of hypertension and the decreased β -adrenergic receptor-mediated response in main renal arteries in the stage of establishment of hypertension. These altered relaxant responses mediated by DA₁-receptors and β -adrenergic receptors found in the main and intrarenal arteries may be associated with the changes in number of receptors or their coupling to adenylate cyclase, rather than being a post-receptor event in the adenylate cyclase/cyclic AMP pathway.