Synthesis and Metabolism of Dopamine in Kidney Slices of Stroke-Prone Spontaneously Hypertensive Rats. Kana Maeda, Makiko Azuma, Yoshitaka Nishimura, Hideaki Higashino, Aritomo Suzuki. Department of Pharmacology, Kinki University School of Medicine, Osaka 589, Japan.

Recent advances in peripheral dopamine research indicate that dopamine plays an important role in regulating the renal circulation and the renal sodium metabolism. In renal tissues, the formation of dopamine from L-dihydroxyphenylalanine (L-DOPA) has been demonstrated to occur mainly in non-neural structures. In the present study, we investigated whether the ability to synthesize dopamine from exogenous L-DOPA is altered in renal tissues of stroke-prone spontaneously hypertensive rats (SHRSP).

Methods

Male SHRSP and Wistar-Kyoto rats (WKY) at 6 (early stage in the development of hypertension), 12 (established hypertension) and 24 (chronic hypertension) weeks of age were used. Under sodium pentobarbital anesthesia (50 mg/kg, i.p.), the rats were exsanguinated through the abdominal aorta. Both kidneys were quickly isolated and then kidney slices 0.5 mm thick were prepared with a tissue slicer (Y.H SLICER®). Kidney slices were preincubated for 60 min in 10 ml warmed (37 °C) and gassed (95% O₂ - 5% CO₂) Krebs-Henseleit solution. After preincubation, kidney slices were incubated for 5, 15, 30 or 60 min in Krebs-Henseleit solution with added L-DOPA (0.1, 1, 10 or 100 μM). After incubation, kidney slices were homogenized with 0.1N perchloric acid containing sodium pyrosulfite, EDTA and 3,4-dihydroxybenzylamine as an internal standard. The kidney homogenates were centrifuged and the supernatant was used for the assay of dopamine, 3,4-dihydroxyphenylacetic acid (DOPAC), 3-methoxytyramine (3-MT), homovanillic acid (HVA), and noradrenaline. These substances were assayed by the gradient reverse-phase high-performance liquid chromatography system including a coulometric array of 16 electrochemical sensors with a refrigerated autosampler (Neurochem®). The protein content of homogenates was determined using the method described by Lowry.

Results and discussion

Incubating of kidney slices from WKY and SHRSP at 6 weeks of age with exogenous L-DOPA (0.1 - 100 μM) resulted in concentration- and time-dependent formation of dopamine, DOPAC, 3-MT, and HVA. However, the amount of newly formed substances did not differ between WKY and SHRSP. Furthermore, there were no significant differences in the amount of dopamine, DOPAC, 3-MT and HVA formed in kidney slices incubated with L-DOPA (1 and 10 μM) for 30 or 60 min between SHRSP at 12 or 24 weeks of age and age-matched WKY. The tissue levels of noradrenaline in kidney slices was not increased in these experiments even when 100 μM L-DOPA was used.

These findings suggest that the formation of dopamine and its metabolism into DOPAC, 3-MT and HVA were similar in kidney slices of SHRSP and WKY at all ages studied.