Decreased Levels of Substance P (SP)- and Methionine Enkephalin (ME)-like Immunoreactivities in Sympathetic Ganglia of Spontaneously Hypertensive Rats. Kazuo Nakamura, Midori Watanabe and Keiji Nakamura. Department of Pharmacology, Nippon Roche Research Center, Kamakura 247, Japan

Recent studies on mammalian sympathetic ganglia accumulate evidences that SP derived from cell bodies in the dorsal root ganglia mediates a slow excitatory post-synaptic potential (slow epsp), while ME presynaptically depressed the SP-mediated slow epsp and probably a cholinergic fast epsp, too. Since the increased sympathetic outflow is present in the prehypertensive age of SHR, the present study has been performed to measure SP and ME contents in sympathetic ganglia and adrenals of SHR and normotensive WKY controls.

In male SHR and WKY at the age of 1–20 weeks, both SP and ME levels in the superior cervical (SCG), stellate (SG) and celiac ganglia (CG), and adrenals were measured by the radio-immunoassay using respective rabbit's anti-sera prepared in the laboratory. Assay limits of SP and ME were each 10 and 30 fmol/tube.

The CG was found to contain the largest SP contents in per organ or protein among these ganglia and adrenals at all ages (1, 4, 20 wks). In 1-week-old rats, SP was not detected in the SG. CG-SP contents per ganglion and per protein were lower respectively in SHR of 4 and 20 weeks old and adult SHR than in corresponding WKY. No significant difference in SP levels was observed in the CG of both groups at one week after birth, and in adrenals at all ages. For ME levels, the CG contained the highest ME contents in all age-groups of 1–20 weeks. The SCG contained ME (per protein) equivalent to CG in all ages examined so far. In 1 and 2 weeks-old SHR, ME levels were lower in SCG, SG, CG and adrenal than those in WKY. Such difference disappeared in animals at age of 5 weeks and thereafter. Plasma levels of ME and SP were determined in femoral arterial blood collected through an implanted cannula. At resting and conscious state, the adult plasma level of both peptides was twice higher than those of young (4, 5 weeks) animals. No difference was obtained in both SHR and WKY. When stress was given to the animal after holding the trunk for a period of 30 s, plasma ME levels were increased by 56% for young WKY and 107% for young SHR, while plasma SP levels were increased by 50–58% for young WKY and SHR. Such increments were not obtained in adult animals.

Thus, the lowered SP levels (per ganglia and protein) in the CG were found in SHR at age of 20 weeks, and the lowered SP contents per ganglia in 4-weeks old SHR, as compared to those of WKY. Since sympathetic ganglion SP originated from the dorsal root ganglia mediates the non-cholinergic slow epsp in sympathetic ganglia, the decreased SP in the CG probably lowers the slow epsp to decrease the SP-mediated excitatory transmission in the CG. Moreover, the present finding may extend to suggest the lowered SP levels in the spinal dorsal horn which receives the SP fiber from dorsal root ganglia, supporting evidence of the elevated pain-threshold in adult SHR. As for lowered ME contents in all sympathetic ganglia and adrenals in SHR at age of 1 and 2 weeks, the lowered ME levels may release ME-mediated presynaptic inhibition of the SP-induced slow epsp and cholinergic fast epsp in sympathetic ganglia and probably in adrenals. Since ChAc in the SG was markedly higher in 1-week old SHR than in WKY, ME-mediated presynaptic inhibition of cholinergic fast epsp might be dominant in the SG as compared to other ganglia and adrenal gland. The decreased ME and elevated ChAc in the SG probably induce cardiac hypertrophy well before the development of hypertension in SHR.

In summary, SP richly present in the CG was significantly lower in adult SHR (20-weeks old) than in WKY, resulting in the decrease in the SP-mediated slow epsp in the ganglia, while ME contents were significantly lowered in all three sympathetic ganglia and adrenal medulla of young SHR (1- and 2-weeks old) than in WKY. The decreased ME contents may release the ME-mediated presynaptic inhibition of SP-induced slow epsp and cholinergic fast epsp in the ganglia and probably in the adrenal gland, thereby enhancing the sympathetic outflow from the CNS to the periphery.