12) Presynaptic Modulation of Norepinephrine Release in the Hypothalamus and Brainstem of Spontaneously Hypertensive Rats. Takao Kubo, Yoshio Goshima, Hiroshi Ueda and Yoshimi Misu, Yokohama City University School of Medicine Yokohama 232.

Brain norepinephrine has been implicated in the development and maintenance of hypertension in several models of experimental hypertension. Norepinephrine release from noradrenergic neurons can be inhibited via presynaptic α_2 adrenoceptors. In this study, the presynaptic α_2 adrenoceptors-mediated inhibitory modulation of noradrenergic neurotransmission was evaluated in the hypothalamic and brainstem slices of spontaneously hypertensive (SHR) and normotensive Wistar Kyoto (WKY) rats, and of deoxycorticosterone-NaCl hypertensive (DHR) and normotensive Wistar (NTR) rats.

SHR at the prehypertensive (4-week-old) and hypertensive (16-week-old) stages were compared with age-matched WKY. For the production of DHR, rats were subjected to left nephrectomy, DOCA (20 mg/kg) was injected subcutaneously twice per week from the 5th week onwards, and 1 % NaCl was substituted for drinking water. These rats were decapitated and the brains removed. The hypothalamus and brainstem (pons/medulla) were dissected out using the method of Glowinski and Iversen, and were cut sagittally. The slices were superfused in an overflow manner at the rate of 0.4 ml/min at 37°C with Krebs solution containing cocaine 2×10^{-5} M. Electrical field stimulation was performed by 30 mA rectangular pulses of 2 msec duration at a frequency of 5 Hz for 3 min through platinum spiral electrodes set up at the two ends of the chamber, using an electrical stimulator with an isolater. Stimulation was applied 30, 60 (S₁) and 90 (S₂) min after the start of superfusion and 3 min samples of the superfusates were successively collected. Yohimbine was added 15 min before the S₂ period of stimulation. The effects of yohimbine were evaluated by S₂/S₁ ratio of evoked amounts. Norepinephrine was measured with high performance liquid chromatography with an electrochemical detector.

In the absence of yohimbine, the S₂/S₁ ratios in the hypothalamus and brainstem were not significantly different between SHR and WKY. At concentrations of 10^{-7} - 10^{-6} M, yohimbine, a selective α_2 antagonist, significantly increased stimulus-induced release of norepinephrine from the hypothalamic and brainstem slices of SHR and WKY. In 16-week-old SHR (175 $\pm$ 3 mm Hg), the effects of yohimbine (10^{-7} M) were significantly decreased in the posterior part of the hypothalamus and increased in the brainstem as compared with those of age-matched WKY (129 $\pm$ 2 mm Hg), respectively, while there were no significant differences in the anterior part of the hypothalamus between 16-week-old SHR and WKY. In 4-week-old SHR (99 $\pm$ 4 mm Hg), the effects of yohimbine (10^{-7} M) were also significantly decreased in the posterior part of the hypothalamus and increased in the anterior part of the hypothalamus as compared with those of age-matched WKY (93 $\pm$ 4 mm Hg), respectively, while there were no significant differences in the brainstem between 4-week-old SHR and WKY. In DHR (182 $\pm$ 4 mm Hg), the effects of yohimbine (10^{-7} M) were significantly decreased in the posterior part of the hypothalamus as compared with those of NTR (115 $\pm$ 2 mm Hg), while there were no significant differences in the anterior part of the hypothalamus and the brainstem between DHR and NTR.

These results suggest that the presynaptic α_2 adrenoceptors-mediated inhibitory modulation of noradrenergic neurotransmission is decreased in the posterior part of the hypothalamus of 4- and 16-week-old SHR and of DHR, and is increased in the anterior part of the hypothalamus of 4-week-old SHR and in the brainstem of 16-week-old SHR. It has been generally thought that an adrenergic system in the posterior hypothalamus has excitatory effects on cardiovascular control and adrenergic systems in the anterior hypothalamus and brainstem have inhibitory effects. Thus, these changes in presynaptic modulation of noradrenergic neurotransmission may be involved in the development or maintenance of hypertension in SHR.