Altered Basal Release and Pressor Effect of L-DOPA in the Rostral Ventrolateral Medulla of Spontaneously Hypertensive Rats. Jin-Liang Yue, Takeaki Miyamae, Hiroshi Ueda and Yoshimi Misu. Department of Pharmacology, Yokohama City University School of Medicine, Yokohama 236, Japan.

We have proposed that L-DOPA is a neurotransmitter in the central nervous system (CNS) (Misu and Goshima: TiPS 14: 119, 1993). Exogenously applied L-DOPA itself produces stereoselective postsynaptic cardiodepressor responses in the nucleus tractus solitarii (NTS) (Kubo et al.: Neurosci Lett 140: 153, 1992) and caudal ventrolateral medulla (CVLM) (Yue et al.: Neurosci Lett 159: 103, 1993). Furthermore, endogenous L-DOPA is released in a transmitter-like manner from in vivo NTS area by aortic nerve stimulation, phenylephrine-induced hypertension and K⁺-elicited depolarization (Yue et al.: Neuroscience, in press). L-DOPA may be a neurotransmitter of baroreceptor afferents and plays an important role in control of blood pressure (BP) in CNS. The rostral ventrolateral medulla (RVLM) receives inputs from various regions including NTS and CVLM and projects directly to the thoracolumbar intermediolateral cell column, which is the main origin of the spinal sympathetic outflow. Increased sympathetic activity of central origin is thought to be a major contributing factor in the initiation and maintenance of hypertension of spontaneously hypertension rats (SHR). We previously reported that L-DOPA is tonically released in a transmitter-like manner and produces stereoselective postsynaptic cardiopressor responses in the rat RVLM (Yue et al.: Brain Res 629: 310, 1993). Here, by using in vivo microdialysis and microinjection techniques, we compared basal release and pressor effect of L-DOPA in RVLM of SHR with those of Wistar Kyoto (WKY) rats.

Fifteen-sixteen-week-old SHR and WKY rats were anesthetized with uretane (1.2 g/kg, i.p.), artificially ventilated with a respirator and then paralyzed with D-tubocurarine (1 mg/kg, i.m.). A dialysis probe (0.5 mm in diameter) for microdialysis or a glass micropipette (50 µm in diameter) for microinjection was stereotaxically inserted into the unilateral RVLM. Ringer solution was perfused at a rate of 1 µl/min. Perfusate was collected every 40 min. L-DOPA in perfusates was measured by HPLC-ECD.

Resting mean BP and heart rate (HR) were elevated in SHR (n = 6), compared to WKY rats (n = 6) (139 ± 4 vs 89 ± 5 mmHg, P < 0.05; 393 ± 9 vs 360 ± 11 beats/min, P < 0.05). By microdialysis in the unilateral RVLM, the basal L-DOPA release became constant in 3 successive samples 2 h after the start of perfusion. This release was higher in SHR than in WKY rats. Tetrodotoxin (TTX, 1 µM) gradually and partially inhibited the release to an approximately similar degree in the two strains. TTX-sensitive L-DOPA release was higher in SHR than in WKY rats. The tonic neuronal release of L-DOPA is enhanced in RVLM of SHR. In addition, L-DOPA (10-600 ng) and L-glutamate (10-300 ng) microinjected into the unilateral RVLM produced dose-dependent increases in BP and HR. The maximum pressor but not tachycardiac responses to low doses of L-DOPA (10 and 30 ng) were greater in SHR than in WKY rats, whereas no differences of pressor and tachycardiac responses to L-glutamate were seen in the two strains. The dose-pressor response-curve for L-DOPA was shifted to the left in SHR. There is high sensitivity of the recognition site for L-DOPA in RVLM of SHR. Presynaptic increase in tonic neuronal release of L-DOPA and postsynaptic sensitization of the recognition site to L-DOPA to elicit pressor responses in RVLM may be involved in the maintenance of hypertension in SHR.