Pathophysiological role of a Novel Vasopressin Receptor (Vp) in isolated SHRSP nephron segments. Kyu Yong Jung, Keiichi Shimamura, Satoru Sunano, and Hitoshi Endou. Department of Pharmacology, Faculty of Medicine, University of Tokyo, Bunkyo-ku, Tokyo 113; and Research Institute of Hypertension, Kinki University, Sayama, Osaka 589.

In addition to renin-angiotensin-aldosterone system, vasopressin (or AVP) is also considered as an important regulator in hypertension. AVP coupled with V2 receptor activates adenylate cyclase, and thus synthesized cAMP regulates sodium and water reabsorption in thick ascending limb of Henle’s loop and collecting tubule, respectively. Recently, we have found a novel vasopressin receptor (Vp) in isolated normotensive rat early proximal tubule (S1). Majority (about 90%) of AVP receptor subtypes in S1 is Vp, and that in medullary thick ascending limb of Henle’s loop (MTAL) and outer medullary collecting tubule (OMCT) is V2. Vp stimulation by AVP inhibits ATP consumption presumably by inhibiting sodium pump. From these observations, this study was aimed to investigate role(s) of Vp receptor under several stages of hypertension using isolated SHRSP nephron segments.

S1, MTAL and OMCT were isolated from collagenase-treated kidney of young (4-5weeks) and adult (12-14 weeks) WKY and SHRSP. AVP (10⁻⁷M)-induced intracellular free calcium ([Ca⁺⁺]i) change was measured using Fura-2. In order to investigate a role of AVP (10⁻⁷M) in ion transport, cellular ATP content was measured by microchemiluminescence method.

AVP transiently increased [Ca⁺⁺]i in adult WKY S1, MTAL and OMCT. AVP-induced [Ca⁺⁺]i transient in adult SHRSP S1 was significantly attenuated compared to adult WKY S1. When adult WKY S1 and MTAL were incubated with AVP in the presence of Na⁺ and absence of exogenous substrates, cellular ATP content in MTAL was significantly low compared to control, whereas the reversed result was obtained in S1. These results indicate that AVP (V2) receptor in MTAL stimulates ATP-consuming active ion transport, but AVP (Vp) receptor in S1 inhibits this. Interestingly, AVP did not change the cellular ATP content in adult SHRSP S1. Similar to WKY MTAL, cellular ATP in SHRSP MTAL was significantly lowered by AVP. Moreover, AVP-induced [Ca⁺⁺]i mobilization was also significantly attenuated in dehydrated rat S1. On the other hand, a role of Vp receptor investigated in young WKY and SHRSP revealed that AVP-induced [Ca⁺⁺]i transient in OMCT was similar to adult WKY and SHRSP. However, [Ca⁺⁺]i increase by AVP in young SHRSP S1 was slightly decreased compared to young WKY S1.

From these results, it is suggested that stimulation of Vp receptor inhibits ATP-consuming active ion transport in normotensive rat S1. However, lack of Vp receptor responsiveness in SHRSP might lead to increase ion transport, and thus to augment cellular volume expansion. And then, this study concludes that Vp receptor could be considered as one of regulators for the development of hypertension in SHRSP.