Spontaneous Contraction of Smooth Muscle in the Internal Carotid Artery of Hypertensive Rats. Keiichi Shimamura, Kazuo Yamamoto, Fumiko Sekiguchi*, and Satoru Sunano. Research Institute of Hypertension, and *Faculty of Pharmaceutical Sciences, Kinki University, Osaka-sayama, 589

Smooth muscle of large arteries in hypertensive rats has been shown to develop spontaneous myogenic activity which is dependent on extracellular Ca and sensitive to voltage-dependent Ca channel blockers. It has also been suggested that Ca influx through voltage-dependent Ca channels is enhanced in smooth muscle of spontaneously hypertensive rats.

In the present study, we examined effect of drugs which are known to have inhibitory action on nonspecific cationic channels, on the spontaneous tonic contraction in endothelium-removed internal carotid arteries from hypertensive rats. Contribution of membrane potential to the contraction was examined with a K channel opener and recording of membrane potential.

Internal carotid arteries were excised from 16 weeks old stroke-prone spontaneously hypertensive rats (SHRSP) and normotensive Wistar Kyoto rats (WKY). Endothelium was removed by rubbing inner surface or perfusion of deoxycholate and spiral preparations were made. Preparations were stretched to 130 % of its relaxed length. Isometric tension of the preparation was measured in a modified Tyrode's solution. Membrane potential was recorded intracellularly with a glass microelectrode.

In the solution containing 2 mM Ca, preparations from SHRSP gradually developed spontaneous active tone. It was inhibited by the removal of extracellular Ca. Preparations from WKY showed negligible tone and removal of extracellular Ca did not affect the tension.

Pinacidil, an ATP-sensitive K channel opener, inhibited the tone. The tone was inhibited by ninety percent replacement of extracellular Na with Tris(hydroxymethyl)aminomethane. Flufenamic acid is a non-steroidal anti-inflammatory drug and 4,4'-diisothiocyanato-stilbene-2,2'-disulfonic acid is a Cl⁻ channel inhibitor. These drugs are known to inhibit non-selective cation channels. The spontaneous tonic contraction of the smooth muscle of carotid artery was inhibited by these drugs. Gadolinium chloride, which is known to inhibit stretch-activated non-selective cation channel also inhibited the spontaneous tonic contraction.

Resting membrane potential of smooth muscle was -45 ± 0.6 and -33 ± 1 mV in WKY and SHRSP, respectively. It was smaller in SHRSP preparation than WKY. Flufenamic acid hyperpolarized the membrane potential significantly in SHRSP.

These results showed that elevation of the active tone in the internal carotid arterial smooth muscle of SHRSP was associated with membrane depolarization. As the depolarization was enough to induce opening of voltage-dependent Ca channel, it may play a key role in development of the tonic contraction. Although the mechanism of membrane depolarization remains unclarified, non-selective cationic movement through the plasma membrane might be involved.