Contractile Responses to 5-Hydroxytryptamine in Isolated Coronary Arteries from Stroke-Prone Spontaneously Hypertensive Rats. Yoshitaka Nishimura and Aritomo Suzuki. Department of Pharmacology, Kinki University School of Medicine, Osaka-fu 589.

5-Hydroxytryptamine (5-HT) is known to induce vasoconstriction in coronary arteries and is considered an important mediator of vasospasm and vasoocclusion associated with atherosclerosis and thrombosis. Coronary arteries from various species including humans contract in response to 5-HT through a mixture of 5-HT₁-like and 5-HT₂ receptors. However, there is little information available concerning the pharmacological characterization of 5-HT-induced contractions in coronary arteries from hypertensive animal models. In the present study, we examined the characterization of 5-HT receptor-mediated contraction in the coronary arteries from stroke-prone spontaneously hypertensive rats (SHRSP).

Method: 6-Month-old male SHRSP and Wistar-Kyoto rats (WKY) were used. The left descending coronary artery was isolated from the heart. The arteries (0.2-0.25 mm in diameter) were cut into rings, 1 mm in length, and mounted horizontally on L-shaped tungsten wires (50 μ M in diameter) in an organ chamber filled with Krebs-Henseleit solution, maintained at 37 °C and aerated with a mixture of 95% O₂ and 5% CO₂. Changes in isometric tension were measured by a force-displacement transducer. All rings were maintained at a resting tension of 150 mg. 5-HT and other agonists were added cumulatively to the organ chamber. Ketanserin and methiothepin were added to the organ chamber 30 min prior to the application of 5-HT.

Results and Discussion: Contractile responses to 5-HT (1-30 nM) were greater in SHRSP arteries than in age-matched WKY arteries, although the maximal response did not differ between the two groups. Ketanserin (100 nM), a 5-HT₂ receptor antagonist, produced biphasic displacement of the concentration-response curves for 5-HT in both groups. The response to low concentrations of 5-HT was resistant to blockade by ketanserin, while the response to high concentrations of 5-HT was antagonized by ketanserin. The ketanserin-resistant contractile responses to 5-HT were greater in SHRSP than in WKY. Methiothepin (100 nM), a 5-HT₁ and 5-HT₂ receptor antagonist, produced a rightward parallel shift in the component of contractile responses induced by 5-HT that was resistant to blockade by ketanserin in both groups. Contractile responses to 5-carboxamidotryptamine (3 nM-1 μ M), a 5-HT₁ receptor agonist, in the presence of ketanserin were greater in SHRSP than in WKY, whereas contractions induced by α -methyl-5-HT (10 nM-30 μ M), a 5-HT₂ receptor agonist, did not differ between the two groups.

These findings suggest that 5-HT contracts the rat coronary artery by stimulation of a mixed receptor population comprised of 5-HT₁-like receptors and 5-HT₂ receptors, and that the contractile response mediated by 5-HT₁-like receptors is enhanced in the coronary artery from SHRSP.