1) Caffeine-induced contraction of smooth muscle of mesenteric artery from hypertensive rat.

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INTRODUCTION: The dependency of contraction on extracellular Ca has been known to be different in the vascular smooth muscle from WKY and SHR or SHRSP. However, little has been studied on the differences in involvements of intracellular stored Ca in the contraction of vascular smooth muscles from WKY and SHRSP. In the present studies, the differences in the stored Ca were examined observing caffeine-induced contraction of smooth muscle of the mesenteric artery.

METHODS: The second branches of the superior mesenteric artery were isolated carefully from 4-month-old male WKY and SHRSP and spirally cut preparations (200 μ m width and 15 mm length) were made. Contractions were observed isometrically in modified Tyrode's solution at 37 °C. High-K solution was made by equimolar replacement of NaCl with KCl. Histological observations were performed with H-E stained preparation under a light microscope, and the wall thicknesses of the preparations were measured by an image processing computer.

RESULTS AND DISCUSSION: Caffeine induced a transient contraction in the smooth muscle of the mesenteric artery both from WKY and from SHRSP. In the presence of Ca, the threshold contraction of caffeine for the initiation of contraction was about 0.1 mM and almost identical in the preparation from SHRSP and WKY. The peak tension was achieved at the concentration of 10 mM. Again, no difference in the concentration for the maximum effect was observed between preparations from SHRSP and WKY. However the developed tension was significantly greater in the preparation from SHRSP. Although the thickness was greater in SHRSP preparation ($56.4 \pm 1.5 \mu$ m) than that of WKY preparation ($40.8 \pm 1.5 \mu$ m), the developed tension was significantly greater even after it was normalized by wall thickness. High-K-induced contracture was also greater in the preparation from SHRSP. However, the preparation from SHRSP showed significantly greater caffeine-induced contraction even when normalized by high-K-induced contracture. The amplitudes of caffeine-induced contraction was 51.5 ± 1.1 % and 39.5 ± 0.8 % of those induced by high-K Tyrode's solution, respectively in SHRSP and WKY preparation. The caffeine-induced contraction decreased by soaking the preparation in Ca-free solution containing EGTA (2 mM) in a time dependent manner. The time course of the decrease was not greatly different in preparations from WKY and SHRSP. However, the contraction at the time when high-K-induced contracture disappeared was slightly but significantly greater in the preparations from SHRSP. The dose-response relation for absolute value of the caffeine-induced contraction in the absence of extracellular Ca was also examined at 10 min after Ca removal. Higher concentration of caffeine was required for the initiation of contraction and the threshold concentration was 1 mM both in SHRSP and WKY preparation. The maximum contraction was achieved at the concentration of 30 mM and, then, the contraction amplitude decreased slightly. The maximum tension induced by 30 mM caffeine was significantly greater in the preparation from SHRSP. Ca-antagonists (verapamil, nifedipine and diltiazem) showed only slight depressing effect on caffeine-induced contraction both in the presence and absence of Ca. These results indicate that caffeine releasable Ca (stored Ca) might be greater in SHRSP vascular smooth muscle but time course of the loss of this Ca fraction after the removal of extracellular Ca is not greatly different in the preparations from both strains.