Effects of Losartan, an Angiotensin II Receptor Antagonist, on Blood Pressure and Plasma Noradrenaline Response in SHR. Yanzhi Hou, Takeshi Tsutsumi, Hirofumi Osada, Disheng Men*, Aiko Matsui* and Yoichiro Matsui*. Division of Cardiology, Showa University, Fujigaoka Hospital, Yokohama 227, *Department of Physiology, Showa University School of Dentistry, Tokyo 142.

We have examined the effects of enalapril, an ACE inhibitor on blood pressure (BP) and plasma noradrenaline (NE) responses in SHR and WKY. Using a microdialysis technique, we continuously measured plasma NE and BP in the same animal. In this paper, we report the effects of losartan (MK-954), a new type (non-peptide) of an angiotensin II receptor antagonist, on BP, heart rate and plasma NE response.

Methods: Sixteen weeks aged SHR and WKY were lightly anesthetized with halothane (0.8-1.2%). Systolic (SBP) and diastolic (DBP) blood pressure were monitored from the carotid artery. Heart rate was calculated from a cardogram. A microdialysis probe was inserted into the jugular vein and perfused with saline. Dialysates were collected continuously every 20 min for three hours. The concentration of NE in the dialysate was measured by HPLC-ECD. Losartan (3 and 10 mg/kg) were injected into the femoral vein. As a control, same volume of saline was injected.

Results: Before experiment, SBP was measured using a tail-cuff method without anesthesia. SBP was 195.1 ± 6.8 in SHR and 118.8 ± 9.6 mmHg (mean ± S.E.) in WKY, respectively. In lightly anesthetized condition by using halothane, SBP was 141.0 ± 3.0 in SHR and 99.0 ± 2.5 mmHg in WKY, respectively. DBP was 88.5 ± 2.8 in SHR and 60.2 ± 2.8 mmHg in WKY, respectively. Concentration of plasma NE was 6.5 ± 0.5 in SHR and 3.6 ± 0.3 (pg/sample) in WKY, respectively. When losartan was administered at a dose of 3 mg/kg, after 20 min, SBP was decreased by 4% and DBP was decreased by 9% (p<0.05) in SHR. However, after 40 min, both SBP and DBP recovered to a control level. Heart rate and concentration of plasma NE were not changed significantly. At a dose of 10 mg/kg, after 20 min, SBP was decreased by 10% and DBP was decreased by 27% (p<0.01) in SHR. After that SBP and DBP were kept almost same level for a long period of time. Concentration of plasma NE was not changed significantly. Heart rate was slightly increased (about 3%). Almost same situation (hypotensive effect) was observed in WKY as SHR. No significant change was observed in heart rate and concentration of plasma NE in WKY.

Conclusion: Losartan had a strong hypotensive effect, especially in DBP. Since no change was observed in plasma NE level, it was considered that losartan did not affect in NE releasing mechanisms.