in the genesis of essential hypertension, effects of digoxin on pressor response to norepinephrine (NE) were studied in 14 normotensive male volunteers (age, 27 ± 2 years, mean $\pm$ SD). NE infusion test ($0.22 \mu\text{g/kg/min}$) was performed before and 90 minutes after intravenous administration of 0.25 mg digoxin. Before and 20 minutes after the start of NE infusion, blood pressure (BP) was measured by sphygmomanometer, cardiac output (CO) by echocardiography, plasma NE concentration (PNE) by the electrochemical method using high power liquid chromatography and intraerythrocytic sodium concentration (ENA) by flame photometry after cell lysis. Total peripheral resistance (TPR) was estimated by mean BP (MBP) and CO.

RESULTS: After digoxin, basal values of BP, CO and TPR were unchanged, but PNE and ENA were increased (0.315 ± 0.137 to $0.405 \pm 0.158 \text{ ng/ml}$, $p < 0.05$; 8.15 ± 0.76 to $8.71 \pm 0.86 \text{ mEq/l}$ cells, $p < 0.01$, respectively). A decrease in CO by NE infusion was unchanged after digoxin. Digoxin augmented an increase in MBP (ΔMBP) and TPR (ΔTPR) by NE infusion ($19.3 \pm 6.2 \text{ mmHg}$, $p < 0.01$; 603 ± 306 to $745 \pm 221 \text{ dynes} \cdot \text{sec} \cdot \text{cm}^{-5}$, $p < 0.01$, respectively). The ratio of $\Delta\text{MBP}/\Delta\text{PNE}$ and $\Delta\text{TPR}/\Delta\text{PNE}$, as the parameters of pressor response and vascular reactivity, respectively, were augmented after digoxin ($p < 0.01$, respectively).

CONCLUSION: The augmented pressor response to NE by digoxin is thought to be caused by increased ΔTPR through an inhibition of Na^+/K^+ ATPase activity in cell membrane. These results suggest that digitalis-like substance may enhance the vascular reactivity to NE, and may play an important role on the genesis of essential hypertension.

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EFFECTS OF OUABAIN ON ADRENERGIC NEURO-TRANSMISSION IN HYPERTENSION

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The purpose of the present study was to determine the role of Na^+/K^+ ATPase activity in the adrenergic neurotransmission in hypertension. The isolated perfused mesenteric vasculatures were prepared in spontaneously hypertensive rats (SHR, Okamoto & Aoki, 7-9 weeks old) and the age-matched Wistar Kyoto rats (WKY). The effects of ouabain, a potent Na^+/K^+ ATPase inhibitor, on the vasoconstriction and norepinephrine overflow from the sympathetic nerve endings were investigated.

(1) The pressor responses and norepinephrine overflow during the electrical nerve stimulation were significantly greater in SHR than in normotensive WKY (10 Hz stimulation: pressor responses, SHR $41.8 \pm 3.2 \text{ mmHg}$, $n=8$, WKY $10.3 \pm 1.0 \text{ mmHg}$, $n=8$, $P < 0.005$, norepinephrine overflow, SHR $1.25 \pm 0.12 \text{ ng/g}$ of wet tissue weight, WKY $0.45 \pm 0.02 \text{ ng/g}$ of wet tissue weight, $P < 0.005$).

(2) Ouabain increased the pressor responses and norepinephrine overflow to the electrical nerve stimulation in the presence of uptake-blocker, desipramine. These facilitatory effects of ouabain were more prominent in SHR than in WKY (ouabain $4.1 \times 10^{-4} \text{ M}$, 10 Hz NE overflow, SHR $172.6 \pm 13.5\%$ of the control NE in the absence of the drug, $n=5$, WKY $124.4 \pm 8.3\%$ of the control, $n=5$, $P < 0.05$).

These results demonstrated that ouabain-sensitive Na^+/K^+ ATPase activity on the presynaptic adrenergic nerve terminals was enhanced in SHR, suggesting that it might be a compensatory mechanism for decreasing intracellular Ca contents in hypertension.

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EPINEPHRINE RELEASE FROM THE PERFUSED ADRENAL MEDULLA OF SPONTANEOUSLY HYPERTENSIVE RATS

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Introduction: Exaggerated responsiveness of the adenosympathetic system to the stress have been reported in spontaneously hypertensive rats (SHR). The present study was designed to observe the changes in local modulation of epinephrine secretion from the adrenal glands of SHR.

Material and methods: Twelve week old SHR and age-matched Wistar-Kyoto rats (WKY) were used. The left adrenal gland was cannulated through the adrenal vein under pentobarbital anesthesia. Retrograde perfusion was immediately started with a modified Krebs-Henseleit solution at room temperature. Platinum ring-electrodes were placed around the adrenal gland. Adrenal gland was stimulated electrically by 1 msec supra-maximal pulses at 5 Hz for 5 min. Acetylcholine (ACh, $10 \mu\text{M}$) was applied in the presence of $1.5 \mu\text{M}$ eserine sulphate to prevent enzymatic hydrolysis of ACh. The perfusate was collected from a small cut in the adrenal cortex every 5 min into a tube containing HCl. Epinephrine release was measured in the presence of different levels of Ca (0.5 , 1.0 , 2.0 mM). Epinephrine was measured by HPLC with electrochemical detector.

Results: In the presence of 2.0 mM Ca, epinephrine secretions induced by electrical stimulation or ACh were greater in SHR than in WKY. The epinephrine secretion responses to electrical stimulation or ACh were diminished in Ca-deficient environment (0.5 mM). Suppression of epinephrine secretion by the fall of Ca concentration in the perfusate was less in SHR compared with WKY.

Conclusions: These results suggest that the epinephrine secretion from adrenal medulla is locally accelerated and less dependant on extracellular Ca in SHR. These adrenal medullary hyperactivity in SHR might be relevant to the pathogenesis of hypertension.

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EVALUATION OF PLATELET NORADRENALINE -IN RELATION TO THE SYMPATHETIC NERVE ACTIVITY-

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The purpose of this study is to clarify whether platelet noradrenaline content (PL-NA) is a useful long-term index for the activity of the sympathetic nervous system.

Material & Methods: 1) Male rabbits, weighing about 4 kg , were continuously infused with noradrenaline (NA) at a rate of $0.77 \mu\text{g/min/kg}$ for 2 hours. PL-NA and plasma NA concentration (P-NA) were measured before and 2, 15, 30, 60, 80 hours after the 2 hours NA infusion. 2) Male Wistar rats, weighing about 250 g , were exposed to cold ($4 \pm 0.5^\circ\text{C}$) for 24 hours. Control rats were kept in room temperature ($25 \pm 0.5^\circ\text{C}$). P-NA, PL-NA and urinary NA (U-NA) were measured in both groups. 3) NA uptake rate of platelets were also measured in patients with essential hypertension (WHO I, II) and the control subjects.

Results: 1) Mean P-NA and PL-NA in rabbits