

## Mechanism Involved in Activation of the Sympathetic Nervous System Induced by Salt-Sensitivity Acquisition in Pressure-Overload Cardiac Hypertrophy

Yoshitaka Hirooka, Koji Ito, Masato Katsuki, Masatugu Nakano

Kyushu University Graduate School of Medical Sciences  
Department of Advanced Cardiovascular Regulation and Therapeutics,  
Department of Cardiovascular Medicine

### Summary

Hypertension and hypertensive hypertrophy are the common basic disorders of the occurrence of heart failure. Those patients often admit the hospitals and it is getting important to take measures for them at the time of aging. In addition, hypertension and heart failure are associated with depression and activation of the sympathetic nervous system is one of the common features between them. We demonstrated that high salt intake elicits sympathoexcitation in mice with pressure overload leading to heart failure. Therefore, we determined to investigate whether inflammatory changes activate mineralocorticoid receptors (MR) in the brain thereby causing sympathoexcitation in hypertensive rats. Stroke-prone spontaneously hypertensive rats (SHRSP) were fed with a high salt diet (8%) for 2 weeks and measured blood pressure, sympathetic activity, proinflammatory cytokines, and MR expression levels. We found that high salt intake induced blood pressure elevation and sympathoexcitation associated with the increased plasma IL-1 $\beta$  concentration. Furthermore, we found that the increase expression levels of TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 in the hypothalamus of the brain. In addition, a marker of MR activation, Sgk1 expression levels were increased in the hypothalamus. Systemic administration of a selective MR blocker, eplerenone, markedly attenuated the increases in blood pressure and sympathetic activity induced by high salt intake. Hypothalamic expression levels of cytokines Sgk1 were also attenuated. These results suggest that inflammatory cytokines and activation of MR in the hypothalamus of the brain increase sympathetic activity in hypertensive rats with high salt intake.