No. 1551

Elucidation of the Mechanism Involved in Acquisition of Salt Sensitivity in Pressure Overload via Cardiac Sympathetic Afferents

Yoshitaka Hirooka, Koji Ito, Risa Takenaka

Kyushu University

Summary

Hypertensive heart disease is the major cause of heart failure with preserved ejection fraction and reveals elevated sympathetic activity. We featured the role of cardiac sympathetic afferent (CSA) reflex. Therefore, the aim of the present stud was to determine whether CSA stimulation could elicit activation of hypothalamic mineralocorticoid (MR)/epithelial Na channels (ENaCs) and inflammatory changes associated with sympathoexcitation evoked by salt loading. Mice with aortic banding were used in the experiments. Epicardial application of capsaicin was performed for CSA stimulation. As a control, epicardial application of ethanol was used. Capsacin treatment increased expression levels of αENaC and TNF-α in the hypothalamus. In contrast, MR and SGK1 expression levels did not change. We found that capsaicin treatment augmented increased in arterial pressure, heart rate, urinary norepinephrine excretion after high salt intake for 5 days. Responses to capsaicin were mediated by TRPV1 because a TRPV1 channel antagonist, capsazepine abolished them. In addition, intracerebroventricular (ICV) treatment with etenercept attenuated capsaicin-induced expression levels of αENaC and TNF-α in the hypothalamus. Also, ICV treatment with etenercept attenuated increases in arterial pressure, heart rate, and urinary norepinephrine excretion. Furthermore, ICV benzamil elicited similar responses. Moreover, capsaicin treatment increased expression levels of αENaC, SGK1, and IL-1β in the hypothalamus. These findings indicate that CSA stimukation leads to an upregulation of hypothalamic αENaC mediated via an increase in TNF-α and results in increased salt sensitivity. We also found that cardiac hypertrophy progressed during 8 weeks after aortic banding, thereafter cardiac function deteriorated. In TRPV1 knockout mice, progression of cardiac hypertrophy was markedly attenuated during the time course, suggesting that CSA stimulation via TRPV1 is responsible for sympathetic activation with progression of cardiac hypertrophy.