No. 1726

Development of Animal Models of Augmented Blood Pressure Variability Induced by High Salt Intake and Identification of the Mechanism and Therapeutic Methods

Johji Kato, Danfeng Jiang, Yukiko Kawagoe, Kenji Kuwasako

Frontier Science Research Center, University of Miyazaki

Summary

Augmentation of blood pressure (BP) variability has been recently recognized as a risk factor for cardiovascular and renal diseases including stroke, heart failure, renal failure, and dementia. BP variability is reportedly associated with aging, high-salt intake, stiffened large artery, and impaired baroreceptor function, assumably mediating the deteriorative effect of high-salt intake on cardiac or renal diseases. In the present study, we have developed rat models of BP variability augmentation induced by high-salt intake in order to clarify the pathophysiology and therapeutic method for salt-sensitive BP variability augmentation. Particularly, our effort is made to identify factors which render BP variability salt-sensitive. Nine-week-old male Wistar rats fed on 0.86% normal-salt or 8% high-salt diet were subcutaneously infused with the low or high dose (24 or 240 pmol/kg/min) of angiotensin II (Ang II) for 14 days without or with oral administration of 15 mg/kg/day hydrochlorothiazide. BP variability was evaluated using a coefficient of variation of blood pressure recorded every 15 min under an unrestrained condition via an abdominal aortic catheter by a radiotelemetry system. High-salt feeding slightly elevated BP level, but had no effect on BP variability. In rats infused with high dose of Ang II, hydrochlorothiazide reduced BP level, without an effect on BP variability. Low dose of Ang II had no effect on BP variability, while being fed on high-salt diet, rats infused with low dose of Ang II showed slightly augmented diastolic BP variability. The present findings suggest that BP variability of Wistar rats fed on normal-salt diet or of those infused with high dose of Ang II is salt-insensitive or fluid volume-independent. Meanwhile, BP variability became partially salt-sensitive in rats infused with low dose of Ang II. As augmentation of BP variability induced by high-salt feeding plus low dose Ang II seems insufficient as a model, our effort will continuously be made to develop rat models by identifying factors which make BP variability highly salt-sensitive.