No. 1234

Mechanism of Salt-Sensitive Hypertension: the Role of Brain Aldosterone and Mineralocorticoid Receptor

Megumi Fujita [1], Chiaki Kawarasaki [1], Kazuhiko Muraoka [1], Toshiro Fujita [2], Katsuyuki Ando [1]

[1] Department of Nephrology and Endocrinology, Faculty of Medicine, The University of Tokyo
[2] Division of Clinical Epigenetics, The University of Tokyo

Summary

We have shown previously that sympathoexcitation by brain oxidative stress mediates arterial pressure elevation in salt-sensitive hypertension. We have also shown that aldosterone-mineralocorticoid receptor activation mediates oxidative stress-induced cardiac and renal dysfunction. Then, we hypothesized that brain aldosterone-mineralocorticoid receptor activation could mediate arterial pressure elevation through brain oxidative stress-induced sympathoexcitation. We used high-salt (8%)-loaded Dahl-salt-sensitive rats (Dahl-S) as the salt-sensitive hypertension model. Sgk-1 and PAI-1 mRNA expression in the isolated hypothalamus was evaluated by real-time quantitative RT-PCR. We examined effects of chronic intracerebroventricular eplerenone, mineralocorticoid receptor blocker on sympathetic nerve activity, arterial pressure, the responses of renal sympathetic nerve activity and arterial pressure to acute intracerebroventricular administration of tempol, an antioxidant, and the hypothalamic oxidative stress level. Salt loading significantly enhanced mRNA expression of Sgk-1 and PAI-1 in the hypothalamus, which suggested mineralocorticoid receptor activation. In salt-loaded Dahl-S, chronic intracerebroventricular eplerenone significantly reduced sympathetic nerve activity and arterial pressure, compared with vehicle-treated group. Reductions in renal sympathetic nerve activity and arterial pressure values elicited by acute intracerebroventricular tempol, and hypothalamic oxidative stress level were significantly suppressed in chronic intracerebroventricular eplerenone-treated group. In conclusion, brain aldosterone-mineralocorticoid receptor activation can be a possible pathogenic background of arterial pressure elevation through brain oxidative stress-induced sympathoexcitation in salt-sensitive hypertension.