No. 1539

Pathophysiological Control of Salt-Sensitive Hypertension through the Modulation of Sodium-Dependent Renal Acetylcholine Release

Shuji Shimizu, Toru Kawada, Tsuyoshi Akiyama, Masafumi Fukumitsu, Michael James Turner

National Cerebral and Cardiovascular Center

Summary

Background: We have already demonstrated that endogenous acetylcholine (ACh) release in the renal cortex is dependent on intracellular sodium concentration of cortical cells. This sodium-dependent ACh release may be impaired in Dahl salt-sensitive rats. Several pharmacological agents, such as ACh esterase inhibitors, may increase interstitial ACh concentrations in the renal cortex and suppress the progression of salt-sensitive hypertension.

Purpose: To investigate the effects of pharmacological agents on renal cortical ACh content of Dahl salt-sensitive rats.

Methods: Male Dahl salt-sensitive rats at 6 weeks of age were fed 8% high salt diet for 8 weeks. An ACh esterase inhibitor, rivastigmine, was orally applied to the rats at a concentration of 50 μg/ml in drinking water. Eight weeks later, these rats were anesthetized with α-chloralose and urethane and the left kidney was extracted. A part of the renal cortex (100 mg) was homogenized into 0.1 M perchloric acid and the supernatant was filtrated. Filtrate ACh content was measured using high-performance liquid chromatography. As a comparison, Dahl salt-sensitive rats and Wistar/ST rats fed normal salt diet were examined.

Results: There were no significant differences in cortical ACh contents between Wistar/ST rats and Dahl salt-sensitive rats under normal salt diet (41.5 ± 1.0 vs. 49.7 ± 1.0 nmol/mg, not significant). In rivastigmine-treated Dahl salt-sensitive rats, ACh content was significantly higher than that in untreated rats (74.3 ± 16.3 vs. 14.8 ± 0.4 nmol/mg, $P<0.05$). Pathological examination demonstrated severer glomerular sclerosis in untreated rats compared with rivastigmine-treated rats.

Conclusions: An ACh esterase inhibitor, rivastigmine, significantly increased cortical ACh contents in Dahl salt-sensitive rats under high salt diet. Pharmacological intervention into cortical ACh release may suppress glomerular damage in the salt-sensitive hypertension.