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# The Role of Sodium-Dependent Renal Acetylcholine Release in Hypertension

Shuji Shimizu, Toru Kawada, Tsuyoshi Akiyama

National Cerebral and Cardiovascular Center

Summary

**Background:** Acetylcholine (ACh) activates endothelial nitric oxide synthesis, causing endothelium -dependent vasorelaxation in renal arteries. Because renal vasodilatation in response to exogenous ACh is attenuated in hypertensive rats, there may be a relationship between the progression of hypertension and endogenous renal ACh release.

**Purpose:** To clarify the mechanism of endogenous renal ACh release and the role of renal ACh in hypertension, a microdialysis technique was applied to the kidney.

**Methods:** A microdialysis probe was implanted into the renal cortex of α-chloralose and urethane anesthetized rabbits and was perfused with the Ringer's solution containing eserine (100 μM) and various pharmacological agents. When high potassium (200 mM), high sodium (500 or 900 mM), $Na^+/K^+$-ATPase inhibitor (ouabain 100 μM), and epithelial $Na^+$ channel blocker (benzamil 300 μM) were locally administered through the probe, dialysate samples were collected. Dialysate ACh concentrations were analyzed using high-performance liquid chromatography.

**Results:** High potassium never increased renal ACh release (1.0 ± 0.2 to 1.0 ± 0.3 nM, not significant). High sodium significantly increased dialysate ACh concentrations in a concentration-dependent manner (500 mM: 1.2 ± 0.4 to 2.4 ± 0.4 nM, $P < 0.05$; 900 mM: 1.1 ± 0.3 to 5.0 ± 1.1 nM, $P < 0.01$). Ouabain significantly increased dialysate ACh concentration (1.2 ± 0.2 to 2.2 ± 0.3 nM, $P < 0.01$). Benzamil significantly decreased dialysate ACh concentrations in both baseline and high sodium (900 mM) conditions (benzamil, $P < 0.01$; high sodium, $P < 0.01$; interaction, $P < 0.01$ by two-way ANOVA).

**Conclusions:** Because high potassium-induced depolarization never increases ACh release, endogenous renal ACh release is mainly dependent on non-neuronal mechanism. An increase in intracellular sodium level enhances this non-neuronal ACh release. Endogenous renal ACh may act as a renoprotective agent against high sodium conditions.