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Exaggerated natriuresis in essential hypertension is not due to increase in renal medullary blood flow

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Background: It has been suggested that in essential hypertension (EH) the exaggerated natriuresis (EN) is associated with an increase in renal medullary blood flow (RMBF). We aimed to measure in mildly hypertensive patients without target organ damage whether EN is associated with changes in RMBF. Methods

7 patients (PT) with EH and 12 controls (CON) were studied, PT after 18 days of drug wash-out including 4 days of low Na⁺ diet. Testing included hemodynamic, hormonal and renal monitoring during i.v. saline loading over 4 h bracketed by non-invasive assessment of RMBF by 15O-water-PET/CT (ref.). This method was verified by measuring RMBF in young healthy males during (i) a control period (ii) Glyceryl nitrate infusion (iii) L-NMMA infusion. Experiments conducted in accordance with the Declaration of Helsinki.

Results: Saline loading increased BP steadily in PT (108 ± 3 to 115 ± 3* mmHg) and transiently in CON (92 ± 2† to 93 ± 2† mmHg). Na⁺ excretion increased 5-fold in PT (33 ± 7 to 150 ± 28* μmol/min) and significantly less in CON (33 ± 5 to 95 ± 13*† μmol/min). RMBF did not change in PT (2.5 ± 0.4 to 2.4 ± 0.5 mL/g tissue/min) or in CON (3.2 ± 0.3 to 3.1 ± 0.2 mL/g tissue/min). Cortical blood flow did not change in PT (3.0 ± 0.4 to 2.7 ± 0.4 mL/g tissue/min), but decreased in CON (4.1 ± 0.3 to 3.7 ± 0.2# mL/g tissue/min). #*P* < 0.05 within group; **P* < 0.001 within group; †*P* < 0.001 between groups.

Conclusion: Mild saline loading, causing 3- and 5-fold increases in Na⁺ excretion, leaves RMBF unchanged.

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Endothelial derived hyperpolarization in renal interlobar arteries

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In small arteries, vascular smooth muscle cells (VSMCs) and endothelial cells (ECs) are connect by myoendothelial junctions (MEJ), usually extending from the EC. Ca²⁺ activated K⁺ channels (IKCa and SKCa) located in the MEJ are suggested to play a role in NO-independent endothelium derived hyperpolarization (EDH) of VSMCs. The IKCa and SKCa channels could affect the VSMC through direct electrical coupling via myoendothelial gap junctions (MEGJ). Alternatively, K⁺ released from the EC into the intercellular space between EC and VSMC could activate VSMC Kir and Na/K-ATPases.

A spatiotemporal model was constructed to simulate possible effect of IKCa and SKCa activation in MEJ. The model suggested that a significant part of the K⁺ current entered the VSMC via MEGJ. The simulation also showed that activation of IKCa and SKCa elevated extracellular K⁺ slightly, which could affect VSMC Kir and Na/K-ATPases.

Experiments were conducted in the wire-myograph using renal interlobar arteries from wild-type and Cx40 knock-out mice. NO synthase and the cyclooxygenase were inhibited using L-NAME and indomethacin. The EDH elicited in renal vessels from wild-type and Cx40 knock-out mice were not significantly different. Inhibition of IKCa and SKCa using TRAM-34 and Apamin significantly reduced EDH in renal vessels from both wild-type and Cx40 KO mice. Inhibition of Kir and Na/K-ATPases reduced EDH in Cx40 KO mice but not in wild-type mice.

We suggest that EDH consists of at least two independent pathways, K⁺ current through MEGJs and increased extracellular K⁺, which can relay the signal from the IKCa and SKCa channels.

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Calcium signaling in coronary artery after reperfusion damage in rat model of acute myocardial infarct

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Background: Ischemia-reperfusion has been demonstrated to increase coronary artery resistance and increase sensitivity toward the potent vasoconstrictor peptide endothelin-1. The increased sensitivity to endothelin-1 is associated with up-regulation of vaso-