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The Mechanism of Salt-Induced Nocturnal Polyuria Focusing on the Brain Sympathetic Nervous Center

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Summary

Nocturnal polyuria is the primary cause of nocturia. We have previously demonstrated that activation of the renal renin-angiotensin system (RAS), associated with reduced nitric oxide (NO) production and excessive salt intake, causes nocturnal polyuria. However, the mechanism by which reduced NO production and excessive salt intake activate the renal RAS remained unclear. This study focused on the involvement of the brain sympathetic nervous center and renal sympathetic nerves in the mechanism of renal RAS activation. The objectives were: (1) to evaluate brain sympathetic nervous center activity in a salt-induced nocturnal polyuria mouse model, and (2) to elucidate the effects of renal denervation (RDN) on renal RAS activity and nocturnal polyuria in this model.

Experiment 1: A salt-induced nocturnal polyuria model was created by administering an NO synthase inhibitor (L-NAME) and a 1% high-salt diet. Brain sympathetic nervous center activity was assessed by c-Fos expression in the paraventricular nucleus (PVN).

Experiment 2: Mice subjected to surgical RDN and sham-operated mice were administered L-NAME and a 1% high-salt diet for 8 weeks. Renal RAS activity was evaluated by intrarenal angiotensinogen (AGT) expression levels, and nocturnal polyuria was assessed by the inactive phase urine volume ratio.

Results 1: In the salt-induced nocturnal polyuria model mice, the number of c-Fos positive cells in the PVN was significantly increased compared to the control group ($P=0.002$), indicating activation of the brain sympathetic nervous center.

Results 2: In the RDN group, intrarenal AGT expression was significantly lower compared to the sham group ($P=0.009$), indicating that renal RAS activity was suppressed. Furthermore, while the inactive phase urine volume ratio increased in the sham group following L-NAME and high-salt diet administration, this increase was significantly suppressed in the RDN group ($P<0.05$).

These results reveal a novel mechanism of nocturnal polyuria induced by reduced NO production and excessive salt intake: activation of the brain sympathetic nervous center enhances renal RAS activity via renal sympathetic nerves. The brain sympathetic nervous center and renal sympathetic nerves are considered potential new therapeutic targets for nocturnal polyuria.