

Kidney dopamine regulates blood pressure, life span

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The neurotransmitter dopamine is best known for its roles in the brain – in signaling pathways that control movement, motivation, reward, learning and memory.

Now, Vanderbilt University Medical Center investigators have demonstrated that dopamine produced outside the [brain](#) – in the kidneys – is important for renal function, blood pressure regulation and [life span](#). Their studies, published in the July *Journal of Clinical Investigation*, suggest that the kidney-specific dopamine system may be a therapeutic target for treating hypertension and kidney diseases such as diabetic nephropathy.

Previous studies had suggested a role for dopamine in regulating kidney function and total body fluid volume, "but how that mechanism works was not clear," said Raymond Harris, M.D., chief of the Division of Nephrology and Hypertension at Vanderbilt.

To explore dopamine's role in the kidney, Harris and Ming-Zhi Zhang, M.D., assistant professor of Medicine at Vanderbilt, eliminated kidney-specific dopamine production in mice (by knocking out a dopamine-generating enzyme only in the kidney) and studied the outcome.

They found that mice lacking kidney dopamine had high blood pressure at baseline and became more hypertensive when they consumed a high-salt diet, suggesting they may be a good model of salt-sensitive (essential) hypertension, Harris said. Alterations in the kidney dopamine

system may predispose individuals to hypertension, he noted.

The investigators also showed that elimination of kidney dopamine increased renin production, which activates the angiotensin II system to increase salt and water reabsorption – and produce hypertension.

"These animals retain salt and water when they don't have sufficient dopamine production in the kidney," Harris said. "Our studies highlight this whole other hormonal system that appears to balance or put the brakes on the renin-angiotensin system."

Currently, the renin-angiotensin system is the major target for treating chronic kidney diseases. Discovering another target – the kidney dopamine system – is exciting, the researchers said. They are exploring whether specific drugs that enhance the kidney dopamine system are effective in blocking hypertension and treating progressive kidney diseases.

The investigators predicted changes in kidney function in the mouse model, but they were "very surprised" to discover that the modified mice only lived about half as long as normal mice (15 months versus 30 months). They found increases in stress-related proteins in the kidney, heart and vasculature, suggesting that elimination of kidney dopamine causes systemic effects, Harris said.

"This kidney-specific dopamine system is not only important for [kidney function](#) and [blood pressure](#) regulation, but also for the overall health of the animal," Harris said. "If the [dopamine system](#) in the [kidney](#) is altered, the animals have a markedly shortened life span."

Provided by Vanderbilt University Medical Center

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