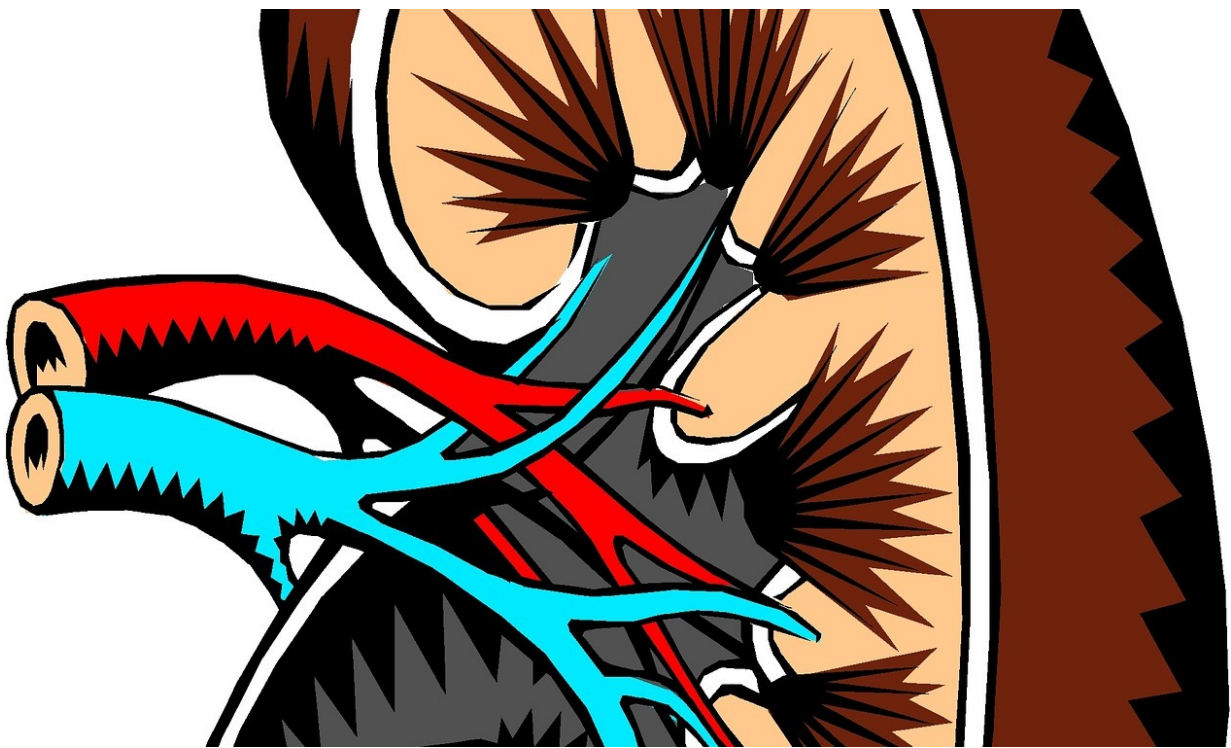


Blocking brain signals detected in the kidney could help unlock future treatments for kidney failure

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Scientists have discovered an important cell signaling pathway in the kidney which if stopped, could hold the key to treating chronic kidney disease as well as other deadly conditions, including heart attack and

stroke.

The pathway was already known to exist in the brain, where it helps to maintain the body's energy balance, but this is the first time it has been found in the kidney.

The pioneering research led by the University of Bristol, published today in *Proceedings of the National Academy of Sciences (PNAS)*—the official journal of the United States' National Academy of Sciences—identified a substance called Neuropeptide Y (Npy), present in high levels in the brain, in the filtering unit of the kidney.

Scientists found Npy in cells called podocytes, which were sending harmful signals and damaging the filtering unit, known as the glomerulus. This caused large amounts of protein to leak into urine, a condition called proteinuria. Often undiagnosed early on, if left untreated the disorder can lead to kidney failure requiring dialysis or a [kidney transplant](#) and it is related to an increased risk of suffering a heart attack or stroke.

Richard Coward, Professor of Renal Medicine at the University of Bristol, said: "Chronic kidney disease affects more than one in 10 of the world's population, claiming millions of lives every year. That makes the discovery of Npy's detrimental potential in the kidney and ways to block it an exciting step forward, which could play a vital role in developing new treatments for proteinuric kidney disease and its associated complications."

Initially the international collaborative study focused on diabetic kidney disease, the leading cause of [kidney failure](#) in the world. It revealed Npy was produced by the podocyte in the kidney as well as the brain. Furthermore, Npy production was massively reduced in diabetic podocyte cells studied in laboratory dishes and Npy levels were also

significantly lower in the glomeruli of patients with diabetes.

"It surprised us because that's the opposite to what happens in the blood circulation in diabetes and other kidney diseases, where Npy levels typically increase. So we wanted to delve deeper and find out what could be happening here and why," Professor Coward said.

To better understand the importance of Npy in the kidney, the research group studied mice that were both able and unable to produce Npy. Findings showed mice lacking Npy were protected from both diabetic and non-diabetic kidney disease. This suggested the local reduction of glomerular Npy initially observed was not causing a problem, but was in fact a protective mechanism to reduce the amounts of local damaging Npy channelled to the kidney.

Researchers went on to identify the precise signaling pathway of harm within the kidney, and found it was happening via a [cell receptor](#) called Npy Receptor 2 (Npy-2R). Having pinpointed the exact damaging pathway, they were determined to discover a way to stop it with medical intervention. So the mice with kidney disease were given a drug to block the Npy Receptor 2, which resulted in them developing much less severe [kidney disease](#).

Professor Coward said: "This is a hugely exciting breakthrough and shows that exploring and finding ways to stop Npy in its tracks really could take us one step closer to beating [chronic kidney disease](#), along with a host of other debilitating conditions. We look forward to advancing this vital work in future research."

More information: Abigail C. Lay et al., "A role for NPY-NPY2R signaling in albuminuric kidney disease," *PNAS* (2020).
www.pnas.org/cgi/doi/10.1073/pnas.2004651117

Provided by University of Bristol

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