
New culprit identified in metabolic syndrome

A new study suggests uric acid may play a role in causing the metabolic syndrome, a cluster of risk factors that increases the risk of heart disease and type 2 diabetes.

Uric acid is a normal waste product that is removed from the body by the kidneys and intestines and is released in the urine and stools. Elevated levels of uric acid are known to cause gout, an accumulation of the acid in the joints. High levels are also associated with markers of the metabolic syndrome, which is characterised by obesity, high blood pressure, and elevated blood sugar and cholesterol levels. But it has been unclear whether uric acid itself is causing the damage or it is simply a by-product of other processes that lead to the dysfunctional metabolism.

New research from the Washington University suggests that excess uric acid in the blood is no innocent bystander. Rather, it appears to be a culprit in disrupting normal metabolism. The research team states that uric acid may play a direct, causative role in the development of the metabolic syndrome. The work showed that the gut is an important clearance mechanism for uric acid, opening the door to new potential therapies for preventing or treating type 2 diabetes and the metabolic syndrome.

Recent research by the senior author, Kelle H Moley, the James P Crane professor of obstetrics and gynecology, and her collaborators has shown that a protein called GLUT9 is an important transporter of uric acid. The team studied mice to learn what happens when GLUT9 stops working in the gut, essentially blocking the body’s ability to remove uric acid from the intestine. In this study, the kidney’s ability to remove uric acid remained normal.

Eating regularly, mice missing GLUT9 only in the gut quickly developed elevated uric acid in the blood and urine compared with control mice. And at only six to eight weeks of age, they developed the hallmarks of the metabolic syndrome: high blood pressure, elevated cholesterol and blood insulin levels, and fatty liver deposits, among other symptoms.

The researchers also found that the drug allopurinol, which reduces uric acid production in the body and has long been used to treat gout, improved some but not all of the measures of metabolic health. Treatment with the drug lowered blood pressure and total cholesterol levels.

Exposure to uric acid is impossible to avoid because it is a normal byproduct of cell turnover in the body. But there is evidence that diet may contribute to uric acid levels. Many foods contain compounds called purines that break down into uric acid. Adding to growing concerns about fructose in the diet, evidence suggests that fructose metabolism in the liver also drives uric acid production.

Switching to foods heavy-laden with fructose over the past 30 years has been devastating, according to Moley. ‘There’s a growing feeling that uric acid is a cause, not a consequence, of the metabolic syndrome. The medical community now knows that fructose directly makes uric acid in the liver. With that in mind, the laboratory is doing further research to study what happens to these mice on a high-fructose diet.’

Source