

Abnormal branched-chain amino acid breakdown may raise diabetes risk

July 5 2018



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In the U.S., about five out of 100 expectant mothers develop gestational diabetes mellitus (GDM), a temporary form of diabetes in which hormonal changes disrupt insulin function. Although GDM is often

symptomless and subsides after delivery, women with a history of it face a seven-fold risk for developing type 2 diabetes.

The biological mechanisms underlying this rise in type 2 diabetes risk are mysterious. But a new study in *Clinical Chemistry* led by Deirdre Tobias, DSc., associate epidemiologist at Brigham and Women's Hospital and Assistant Professor at Harvard Medical School, suggests that the irregular metabolism of branched-chain amino acids—components of proteins found in many foods—may be partially to blame for progression to type 2 diabetes.

Tobias and her team of researchers assessed reported diets and [blood samples](#) collected during the Nurses' Health Study II, an investigation of chronic disease risk in women that was carried out from 1989 and continues today. They looked at the data from 347 women with histories of GDM, roughly half of whom later developed type 2 diabetes. The researchers calculated the women's levels of branched-chain amino [acid](#) intake using published guidelines for nutrient content. Using mass spectrometry, they also measured the levels of branched-chain amino acids in the blood samples that were collected prior to type 2 diabetes development during the period of 1996-1999.

The researchers found that women with a history of GDM who later developed type 2 diabetes had higher levels of branched-chain amino acids in their blood, regardless of their [dietary intake](#). That suggests that greater consumption of branched-chain amino acids may increase the risk for type 2 diabetes, but only if an individual's ability to properly metabolize them is impaired.

"If your dietary intake is high, but you can clear these normally from circulation, then you don't seem to be at a higher type 2 diabetes risk," said Tobias.

Researchers cannot yet fully characterize the specific pathway of this impaired metabolism, but the abnormality seems to result in a buildup of circulating branched-chain amino acids, which have a detrimental downstream effect on insulin function.

Branched-chain amino acids are essential amino acids, meaning that they can only be obtained from food. They play important roles in immune and neurological function, and they exist in a wide variety of foods. Tobias emphasized that branched-chain amino acids are not necessarily unhealthy. More research is needed to determine whether lowering dietary intake of them can lower type 2 diabetes risk in people with abnormal metabolism.

"From a practical point of view, branched-chain amino acids are difficult to avoid," said Tobias. "They are found in so many protein sources, both healthy and less healthy."

Tobias and her team hope that early detection of abnormally high branched-chain amino acid blood concentrations may one day enable earlier interventions for those at risk for type 2 [diabetes](#). They suggest it will take further research to determine if tests to detect these levels should become standard procedures during doctor's appointments.

More information: Deirdre K. Tobias, Clary Clish, Samia Mora, Jun Li, Liming Liang, Frank B. Hu, JoAnn E. Manson, and Cuilin Zhang. "Dietary Intakes and Circulating Concentrations of Branched-Chain Amino Acids in Relation to Incident Type 2 Diabetes Risk Among High-Risk Women with a History of Gestational Diabetes Mellitus. *Clinical Chemistry*. In Press.

Provided by Brigham and Women's Hospital

Citation: Abnormal branched-chain amino acid breakdown may raise diabetes risk (2018, July 5) retrieved 20 March 2024 from <https://medicalxpress.com/news/2018-07-abnormal-branched-chain-amino-acid-breakdown.html>

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