How diabetes might lead to Alzheimer's: Study suggests the liver is key

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Credit: Human Brain Project

New research conducted in mice offers insights into what's going on at the molecular level that could cause people with diabetes to develop Alzheimer's disease.

The study adds to a growing body of research on the links between type

2 diabetes and Alzheimer's disease, which some scientists have called "type 3 diabetes." The findings suggest that it should be possible to reduce the risk of Alzheimer's by keeping diabetes well controlled or avoiding it in the first place, according to researchers.

Narendra Kumar, an associate professor at Texas A&M University in College Station, led the study.

"We think that diabetes and Alzheimer's disease are strongly linked," Kumar said, "and by taking preventative or amelioration measures for diabetes, we can prevent or at least significantly slow down the progression of the symptoms of dementia in Alzheimer's disease."

Kumar presents the new research at Discover BMB, the annual meeting of the American Society for Biochemistry and Molecular Biology, held March 23–26 in San Antonio.

Diabetes and Alzheimer's are two of the fastest-growing health concerns worldwide. Diabetes alters the body's ability to turn food into energy and affects an estimated one in 10 U.S. adults. Alzheimer's, a form of dementia that causes progressive decline in memory and thinking skills, is among the top 10 leading causes of death in the United States.

Diet is known to influence the development of diabetes as well as the severity of its health impacts. To find out how diet could influence the development of Alzheimer's in people with diabetes, the researchers traced how a particular protein in the gut influences the brain.

They found that a high-fat diet suppresses the expression of the protein, called Jak3, and that mice without this protein experienced a cascade of inflammation starting with the intestine, moving through the liver and on to the brain. Ultimately, the mice showed signs of Alzheimer's-like symptoms in the brain, including an overexpressed mouse beta-amyloid

and hyperphosphorylated tau, as well as evidence of cognitive impairment.

"Liver being the metabolizer for everything we eat, we think that the path from gut to the brain goes through liver," Kumar said.

His lab has been studying functions of Jak3 for a long time, he added, and they now know that the impact of food on the changes in the expression of Jak3 leads to leaky gut. This in turn results in low-grade chronic inflammation, diabetes, decreased ability of the brain to clear its toxic substances and dementia-like symptoms seen in Alzheimer's disease.

The good news, according to Kumar, is that it may be possible to stop this inflammatory pathway by eating a healthy diet and getting blood sugar under control as early as possible. In particular, people with prediabetes—which includes an estimated 98 million U.S. adults—could benefit from adopting lifestyle changes to reverse prediabetes, prevent the progression to type 2 diabetes and potentially reduce the risk of Alzheimer's.

More information: Abstract: Kinases in Gut-Liver-Brain Communication and Neuroinflammation

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