

Diabetes medications may reduce Alzheimer's disease severity

1 November 2018



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People with Alzheimer's disease who were treated with diabetes drugs showed considerably fewer markers of the disease—including abnormal microvasculature and disregulated gene expressions—in their brains compared to Alzheimer's patients without treatment for diabetes, Mount Sinai researchers report.

Results of the study will be published in *PLOS One* online on November 1st at 2PM.

This is the first study to examine what happens in the pathways of both brain tissue and endothelial cells—the cells lining blood vessels—in the brains Alzheimer's patients treated with diabetes medication. The results of the study will inform future Alzheimer's disease studies and potential new therapies targeting specific cells, since they suggest that targeting the brain's capillary system could have beneficial effects in Alzheimer's patients.

Many elderly people with diabetes have brain changes that are hallmarks of Alzheimer's. Despite this linkage, two previous Mount Sinai studies on brain tissue found that the brains of people with

both Alzheimer's disease and diabetes had fewer Alzheimer's lesions than the brains from people with Alzheimer's disease without diabetes. The results suggested that anti-diabetes medications had a protective effect on the brains of Alzheimer's disease patients.

To determine what happens at the molecular level, this Mount Sinai research team developed a method to separate brain capillaries from the brain tissue of 34 people with Alzheimer's and type 2 diabetes who had been treated with anti-diabetes drugs and compare them to tissue from 30 brains of people with Alzheimer's without diabetes and 19 brains of people without Alzheimer's or diabetes. (Because most people who have diabetes are treated with insulin or oral medications, the scientists were unable to compare their results to brain tissue from people with Alzheimer's disease and diabetes who were not treated with anti-diabetes drugs.)

Then, they examined the vessels and brain tissue separately to measure Alzheimer's Disease associated changes in molecular RNA markers for brain capillary cells and insulin signaling.

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The levels of about half of these markers were reduced in the vessels and brain tissue in the group with Alzheimer's and diabetes. The great majority of the RNA changes seen in Alzheimer's disease were cells—the cells lining blood vessels—in the brains of absent in those Alzheimer's patients who had been Alzheimer's patients treated with diabetes

"The results of this study are important because they give us new insights for the treatment of Alzheimer's disease," said the study's senior author, Vahram Haroutunian, Ph.D., Professor of Psychiatry and Neuroscience at the Icahn School of Medicine at Mount Sinai.

"Most modern Alzheimer's treatments target amyloid plaques and haven't succeeded in effectively treating the disease," said Dr.



Haroutunian. "Insulin and diabetes medications such as metformin are FDA approved and safely administered to millions of people and appear to have a beneficial effect on people with Alzheimer's. This opens opportunities to conduct research trials on people using similar drugs or on drugs that have similar effects on the brains' biological pathways and cell types identified in this study."

Provided by The Mount Sinai Hospital APA citation: Diabetes medications may reduce Alzheimer's disease severity (2018, November 1) retrieved 15 June 2021 from https://medicalxpress.com/news/2018-11-diabetes-medications-alzheimer-disease-severity.html

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