# Changes in epigenetic DNA functions reveal how diabetes predisposes individuals to Alzheimer's

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Diabetes and dementia are rising dramatically in the United States and worldwide. In the last few years, epidemiological data has accrued showing that older people with diabetes are significantly more likely to develop cognitive deterioration and increased susceptibility to onset of dementia related to Alzheimer's disease. Now, a research team led by Giulio Maria Pasinetti, MD, PhD, the Saunders Family Chair and Professor of Neurology at the Icahn School of Medicine at Mount Sinai, discovered a novel mechanism through which this may occur. The results are published online Oct. 23, in the journal *Diabetes*.

Dr. Pasinetti and colleagues pinpointed changes in post-mortem brains of human subjects. They reported that gene expression was dysfunctional in the brains of diabetic human subjects, and this increase was associated with reduced expression of important molecules that play a critical role in maintaining the structural integrity of brain regions associated with learning.

Excited by this finding, Dr. Pasinetti reasoned that if the hypothesis was correct, similar conditions should be repeated in the laboratory by inducing diabetes in mice genetically predisposed to developing Alzheimer's type memory deterioration.

In fact, Dr. Pasinetti's laboratory confirmed this prediction in the mouse model, supporting the hypothesis that diabetes, through epigenetic

changes in the brain, may casually promote onset and progression of Alzheimer's disease. Epigenetic changes are chemical changes in DNA that effect gene expression, but don't alter the actual genetic code.

"This new evidence is extremely intriguing, given that approximately 60 percent of Alzheimer's disease patients have at least one serious medical condition associated with diabetes," said Dr. Pasinetti. "What this adds is much needed insight into the potential mechanism that might explain the relationship between diabetes and Alzheimer's disease onset and progression by mechanisms through which DNA functions."

The discovery in Dr. Pasinetti's laboratory has staggering societal implications. More than 5 million are affected by Alzheimer's disease dementia, and the disease incidence is expected to skyrocket in the three decades as the population ages.

"The next question we must ask is how we can translate this into the development of novel disease prevention and treatment strategies," Dr. Pasinetti added. "If we can find out how DNA epigenetic modification can be manipulated pharmacologically, these studies will be instrumental in the formulation of novel treatments and possible preventative strategies in Alzheimer's disease.

Provided by The Mount Sinai Hospital