Researchers have long known that people with diabetes have a higher risk of developing Alzheimer's disease than other people. What researchers couldn't explain was why. But now scientists at Mt. Sinai School of Medicine say they may have some clues.

In their previous studies, Mt. Sinai psychiatrist Michal Beeri and her team discovered that people with diabetes in midlife had up to three times the risk of developing dementia 35 years later. Building on that work for their current study, which Beeri presented Monday at the International Conference on Alzheimer's Disease in Chicago, researchers analyzed samples of brain tissue from 248 patients, stored in the Mt. Sinai Brain Bank. Detailed medical histories, including medications taken, were available for all patients. Beeri matched 124 patients with diabetes with 124 non-diabetic patients, who were similar to the first group in age, sex and stage of dementia at death.

Compared with patients who never developed diabetes, patients who had the disease but took insulin along with one additional medication to control blood sugar (typically metformin or glyburide) had 80% fewer brain-clogging amyloid plaques in their brain. Build up of these protein plaques, which are one of the hallmarks of Alzheimer's disease, can interfere with normal communication between nerve cells and cause deficits in memory and cognition. "The group on combination therapy had a very, very low load of neuritic plaques," Beeri says. "Their brains looked almost like normal people." The medications did not, however, do much to reduce the number of tangles — the fibrous nerve nets that are another defining characteristic of the memory-robbing disease — in the brains of Alzheimer's patients.

Beeri and her group are already trying to figure out how — and why — the combination therapies might curb plaque formation but leave the tangles alone. One theory is that the drugs normalize the communication network of insulin receptors, which go awry in the Alzheimer's brain, somehow restoring those pathways to as close to normal as possible, while clearing out the damaging plaques that form when the network malfunctions. "Our hypothesis is that with the combination therapy, the gene and protein
expression of these Alzheimer's patients might be close to that of normal people who don't have Alzheimer's at all," she says. Beeri stresses that it's far too early to recommend that patients showing early signs of Alzheimer's start to take insulin with metformin or glyburide. But, she says "I am hoping that this sheds light on a potentially new mechanism for insulin's role in controlling the disease and lead us to new therapies."