Insulin could be Alzheimer's therapy

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Research by UB's Paresh Dandona shows that a low dose of insulin suppresses the expression of proteins involved in the pathogenesis of Alzheimer's disease. Credit: Doug Levere

A low dose of insulin has been found to suppress the expression in the blood of four precursor proteins involved in the pathogenesis of Alzheimer's disease, according to new clinical research by University at Buffalo endocrinologists. The research, published in March online in the *Journal of Clinical Endocrinology and Metabolism*, suggests that insulin could have a powerful, new role to play in fighting Alzheimer's disease.

"Our results show clearly that insulin has the potential to be developed as a therapeutic agent for Alzheimer's, for which no satisfactory treatment is currently available," says Paresh Dandona, MD, PhD, UB distinguished professor of medicine in the School of Medicine and Biomedical Sciences and senior author on the study.

One of the four proteins shown in the study to be suppressed by insulin is a precursor to beta amyloid, the main component of plaques considered the hallmark of Alzheimer's disease.

The findings also demonstrate for the first time that the four precursor proteins studied are expressed in peripheral mononuclear cells, white blood cells that are an important component of the immune system.

The paper builds on the UB researchers' earlier work showing that insulin has a potent and rapid anti-inflammatory effect on peripheral mononuclear cells. It also builds on the well-known association between obesity, type 2 diabetes and chronic low-grade inflammation, as well as insulin resistance, all conditions that manifest a significantly increased prevalence of Alzheimer's disease.

In the study, 10 obese, type 2 diabetic patients were infused with two 100 ml units of insulin per hour over a period of four hours. The patients were all taking oral drugs to treat their diabetes; none of them were taking insulin or any antioxidant or nonsteroidal anti-inflammatory drugs. The control group received 5 percent dextrose per hour or normal saline solution.

The low-dose insulin was found to suppress the expression of amyloid precursor protein, from which beta amyloid is derived. It also suppressed presenilin-1 and presenilin-2, the two subunits of an enzyme that converts amyloid precursor protein into beta amyloid, which forms the amyloid plaques. Insulin also suppressed glycogen synthase kinase, which phosphorylates, or adds on another phosphate group, to another neuronal protein, tau, to form the neurofibrillary tangles, the other important component of Alzheimer's disease in the brain.

"Our data show, for the first time, that the peripheral mononuclear cells express some of the key proteins involved in the pathogenesis of Alzheimer's disease," says Dandona. "They demonstrate that these cells can be used for investigating the effect of potential Alzheimer's disease therapies on key proteins involved in the disease.

"Even more importantly, it is likely that insulin has a direct cellular effect on these precursor proteins while also exerting its other anti-inflammatory actions," he continues. "If this effect of insulin proves, in larger studies, to be systemic, then insulin may well be a potential therapeutic agent in treating Alzheimer's disease. The challenge is to deliver insulin directly into the brain, thus avoiding its hypoglycemic effect."

Fortunately, Dandona says, a previous preliminary study has shown that intranasal delivery of insulin can lead to its entry into the brain along the olfactory nerves and that its administration may improve cognitive function in patients with Alzheimer's disease. However, he cautions, the mode of action is not known.

"Our study provides a potential rational mechanism," he says.

Provided by University at Buffalo