New study expands range of potential Alzheimer's drugs

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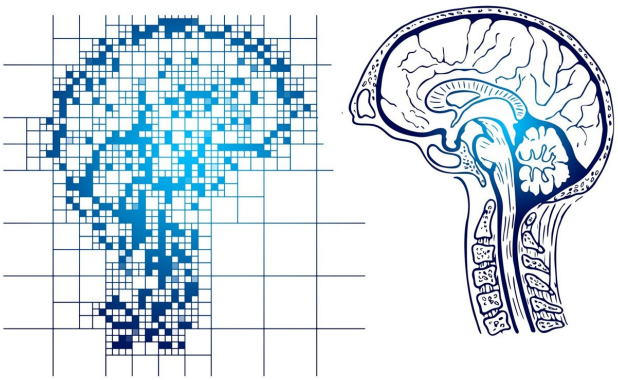

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Alzheimer's disease is associated with a reduction of insulin receptors in brain microvessels, which may contribute to brain insulin resistance and the formation of amyloid plaques, one of the disease's hallmarks. That's according to a study published today in the journal *Brain* by a team from Université Laval and Rush University Medical Center in Chicago.

The work leading to the discovery was headed by Frédéric Calon, a professor at the Faculty of Pharmacy and a researcher at the Institute of Nutrition and Functional Foods and the CHU de Québec–Université Laval Research Center.

The findings could affect the search for new Alzheimer's drugs. "Several clinical trials are underway to assess the efficacy of diabetes drugs for Alzheimer's disease," said Professor Calon. "Our study shows that drugs do not need to cross the blood–brain barrier of microvessels to affect brain insulin resistance. Instead, they can target insulin receptors located in cerebral microvessels. That expands the range of drugs that could be tested for Alzheimer's."

The research was made possible by a longitudinal study that began in 1993 and involves about 1,100 members of some 30 religious congregations in the United States. The participants have agreed to undergo annual medical and psychological tests and donate their brains after death. The *Brain* article is based on data from 60 deceased individuals who participated in this extensive study.

Examination of their brains revealed that:

- Insulin receptors are found primarily in blood microvessels, not neurons, as previously thought.
- Alpha-B insulin receptor subunits were less prevalent in the microvessels of people diagnosed with Alzheimer's.
- Cognitive test scores were lower in subjects with fewer alpha-B insulin receptors in their microvessels.
- Subjects with fewer alpha-B insulin receptors in their microvessels had more beta-amyloid plaques in their brains.

Experiments carried out by the researchers on transgenic mice used to study Alzheimer's disease showed that the quantity of alpha-B receptors in microvessels decreased with age and disease progression.

"Our findings suggest that the loss of alpha-B insulin receptors in brain microvessels contributes to insulin resistance in the brain and cognitive decline in people with Alzheimer's disease," Professor Calon said.

These findings support the idea that Alzheimer's is a neurodegenerative disease with a strong metabolic component. "Metabolic dysfunction exacerbates Alzheimer's, and Alzheimer's amplifies the metabolic problem. It's a vicious circle," said Professor Calon.

Provided by Laval University

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