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## Is Alzheimer's a Form of Diabetes?

By Catherine Guthrie

When the body refuses to make insulin, the condition is called type 1 diabetes; when the body mismanages the hormone, it's known as type 2. Now, scientists report new evidence linking insulin to a disorder of the brain: when the brain prevents the hormone from acting properly, the ensuing chemical imbalance may help trigger Alzheimer's disease. The correlation is so strong that some researchers are calling Alzheimer's disease "type 3" diabetes.

In the body, insulin helps convert food into cellular energy. But the brain has other uses for insulin, namely as a means to learn and make new memories. Here's how it works: At synapses, the spaces across which brain cells communicate and where memories are conceived, neurons reserve special parking spots just for insulin. When the hormone pulls in, a connection is made that enables new memories to form. Since new memory formation is one of the first things to go awry in people with early stages of the disease, this insulin-initiated process may hold the key to decoding the mystery of Alzheimer's.

In August, a team of scientists at Northwestern University were the first to show why the brain's "memory function" fails in the face of an insulin shortage. The group's prior research had already pinpointed the culprit: toxic proteins called amyloid beta-derived diffusible ligands (ADDLs, for short), which are known to pile up in the brains of people with Alzheimer's. Scientists also knew that Alzheimer's patients' brains have lower levels of insulin and are insulin resistant. But what the Northwestern team discovered is the molecular mechanism behind that resistance: when ADDLs bind to neurons at synapses, they obliterate the receptors that are normally reserved for insulin. Without those parking spaces on the brain cells' surface, insulin has no place to connect, and memory fails.

"We now understand that the function of insulin at those synapses is to modulate and influence the underlying cellular structure of memories," says William Klein, professor of neurobiology and physiology at Northwestern University and a co-author of the study published online by the [FASEB Journal](#). "What we have here is a striking phenomenon that may ultimately explain why the brains of people with Alzheimer's disease are insulin resistant and how that ties into memory."

Researchers hope these findings will help shape future research in Alzheimer's therapy — perhaps in the development of drugs that can make brain cells' insulin receptors more responsive to the hormone, or in the application of type 2 diabetes drugs, which address insulin resistance, to Alzheimer's.

The notion that Alzheimer's disease might be a neuroendocrine disorder, akin to diabetes, isn't entirely new; it first showed up in the scientific literature roughly 20 years ago, but the idea petered out. In 2005, Suzanne la Monte, a neuropathologist at Brown University Medical School, revisited the idea. Based on two of her discoveries — that the brain makes its own insulin and that Alzheimer's disease depletes insulin — she coined the disease process "type 3" diabetes.

Still, referring to Alzheimer's disease as "type 3" diabetes is controversial, especially within the diabetes community. Alzheimer's disease is a complication of diabetes, not a unique form of the disease, says Dr. Sue Kirkman, vice president of clinical affairs for the American Diabetes Association. "Nevertheless," she says, "this is primarily a semantic argument."

The terminology aside, both diseases share many traits and risk factors, including high cholesterol, high blood pressure, and metabolic disorders. So, de la Monte sees the semantic "splitting of hairs" as a good thing. "People are arguing about small parts of the bigger story," she says. "At the end of the day, these conversations will help us to better understand both diabetes and Alzheimer's disease."

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