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HEALTH BEAT: NEUROBIOLOGY

Researchers deem Alzheimer's a Type 3 diabetes

By Bonnie Kath
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Sometimes it's better if great minds don't think alike. Neurobiologists with decidedly different interests recently collaborated at Northwestern University and came up with new evidence about Alzheimer's disease, a form of dementia that affects about 5 million Americans. They now consider it a Type 3 diabetes.

Wei-Qin Zhao came to Northwestern as a visiting professor who had shown in published research that insulin receptors in the brain play a critical role in learning and memory. There she met William Klein, professor of neurobiology and physiology in the Weinberg College of Arts and Sciences and a member of the Cognitive Neurology and Alzheimer's Disease Center. He had recently identified the toxin that harms the brain in Alzheimer's, the first symptom of which is an inability to store new memories.

The two, along with professors Fernanda De Felice and Pascale Lacor and other colleagues, worked together to discover that this toxin does its damage by causing the brain to become insulin resistant. Just as Type 2 diabetes occurs when the body becomes insulin resistant, Alzheimer's would be a Type 3 diabetes.

This team studied healthy nerve cells from the brain's hippocampus region, growing in culture dishes, and they observed abundant insulin receptors. "If you look closely at a high-resolution [image], you'll see that they are at synapses," Klein said. "Before we added the ADDLs [toxins], they all had insulin receptors." But with the toxin added to the culture dishes, "the insulin receptors disappeared from their surfaces."

"Whenever insulin can bind to a receptor, it sticks very tightly, and this turns on those insulin receptors; and that's essential for memories to form. That's the normal physiological process. But now, on the other hand, if we have ADDLs [binding] -- these are the toxins that are building up in Alzheimer's brains -- the insulin receptors are removed from the membrane. There's nothing [for the insulin] to stick to, ... and memories cannot form."

As a double check, they introduced insulin into the cultures and found that there was no insulin-receptor response. However, his team did observe that insulin receptors were still present inside the nerve cells, but they no longer reached the surface. "In our theory, in the early stages of Alzheimer's disease, it's not a nerve-cell death phenomenon. It's a signaling phenomenon. ... It should be possible to reverse that early memory failure."

Tribune photo by Yvette Marie Dostatni
Professors Wei-Qin Zhao and William Klein were on a team that found that Alzheimer's disease acts like a Type 3 diabetes.

Klein's work suggests two potential therapies. "[Researchers] are looking at drugs that are given to Type 2 diabetics that increase the ability of cells to respond to insulin. It makes the insulin receptors more abundant or more lively."

Other scientists are working on an anti-ADDL therapy. "There are a number of pharmaceutical companies that ... want to develop antibodies that target ADDLs and neutralize and eliminate them from the brain."

The toxic ADDLs, or amyloid beta-derived diffusible ligands, are the result of an overproduction of the amyloid beta protein. The body can't clear away this protein fast enough, and it binds itself into small clumps and attaches to the synapses in the brain's hippocampus and cortex regions. The plaques that are the hallmark of Alzheimer's disease are also made from this protein, but many researchers now believe that these plaques could be the body's attempt to limit the damage by locking the toxins into immovable masses.

"[Klein's work] is like finding the missing piece of a jigsaw puzzle," said Dr. Norman Relkin, associate professor of clinical neurology and neuroscience at Cornell University. "It brings together two areas that have been proven reasonably well. That's what's exciting about it."

Relkin is working to find a new therapy for Alzheimer's disease using human antibodies.