Research shows diabetes drug improves memory

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An FDA-approved drug initially used to treat insulin resistance in diabetics has shown promise as a way to improve cognitive performance in some people with Alzheimer's disease.

Working with genetically engineered mice designed to serve as models for Alzheimer's, University of Texas Medical Branch at Galveston researchers found that treatment with the anti-insulin-resistance drug rosiglitazone enhanced learning and memory as well as normalized insulin resistance. The scientists believe that the drug produced the response by reducing the negative influence of Alzheimer's on the behavior of a key brain-signaling molecule.

The molecule, called extracellular signal-regulated kinase (ERK), becomes hyperactive both in the brains of Alzheimer's patients and in the mice at a disease stage corresponding to mild cognitive impairment in human Alzheimer's. This excessive activity leads to improper synaptic transmission between neurons, interfering with learning and memory.

Rosiglitazone brings ERK back into line by activating what's known as the peroxisome proliferator-activated receptor gamma (PPARγ) pathway, which interacts with genes that respond to both PPARγ and ERK.

"Using this drug appears to restore the neuronal signaling required for proper cognitive function," said UTMB professor Larry Denner, the lead author of a paper describing this work now online in the Journal of

Neuroscience. "It gives us an opportunity to test several FDA-approved drugs to normalize insulin resistance in Alzheimer's patients and possibly also enhance memory, and it also gives us a remarkable tool to use in animal models to understand the molecular mechanisms that underlie cognitive issues in Alzheimer's."

ERK dysfunction in the Alzheimer's mouse model was discovered several years ago by UTMB associate professor Kelly Dineley, senior author of the *Journal of Neuroscience* paper. But putting together the protein, gene and memory pieces of the puzzle required a multidisciplinary translational research team including animal cognitive neuroscientists, biochemists, molecular biologists, mass spectrometrists, statisticians and bioinformaticists.

"We were extraordinarily lucky to have this diverse group of experts right here on our campus at UTMB that could coalesce to bring such different ways of thinking to bear on a common problem," Denner said. "It was quite a challenge to get all of these experts communicating in a common scientific language. But now that we have this team working, we can move on to even more detailed and difficult questions."

Now the UTMB research team and other investigators across the world are starting clinical trials to investigate the value of therapies for insulin resistance in early-stage Alzheimer's disease in humans.

Provided by University of Texas Medical Branch at Galveston

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