Changes in genetic function in the brain linked to Alzheimer's

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Changes in the epigenome, a structure that controls the function of genes, were found in the brains of Alzheimer's patients.

These epigenetic changes can be caused by exposure to environmental toxicants or lifestyle behaviors, according to a study out of the University of Michigan School of Public Health. If researchers can establish a causal link between epigenetic changes and toxicants, it could lead to new treatments, or even the prevention of Alzheimer's disease. This paper did not look at specific toxicants, but future studies in this body of research will, said Laura Rozek, assistant professor in the SPH and study co-author.

Further, these epigenetic changes, which cause genes to behave differently over a person's lifetime, could be reversible. The researchers found higher rates of a kind of an epigenetic change called methylation in genes located in the brains of people with Alzheimer's, said Rozek, who also has an appointment in the Department of Otolaryngology at the U-M Health System.

"Our next step is to look at exposures that occurred earlier in life and try to link those exposures to the epigenetic changes we saw in the brain," Rozek said. "That way we may find evidence that toxicants are linked to the epigenetic changes that are present in the brains in the people with Alzheimer's."

In the study, researchers did a postmortem comparison of the brains of 50 subjects, half with late onset Alzheimer's, said Dana Dolinoy, assistant professor in the U-M SPH and study co-author. Lower methylation and higher expression of the TMEM59 protein were associated with the Alzheimer's subjects, which suggests that the TMEM59 protein could be a good therapeutic target to prevent and treat Alzheimer's, Rozek said.

"If there are epigenetic changes in the brain they are potentially modifiable, there are probably ways to reverse these changes," Rozek said. "It may be a good biomarker to target for drug therapy for late onset Alzheimer's."

Researchers looked only at late onset Alzheimer's, which is vastly more common than early onset Alzheimer's, which affects only about 2 percent of people and sets in before age 60.

Scientists have identified several genes that may increase a person's risk for developing Alzheimer's. The same genes can have different outcomes in different people. So, other factors must play a role in

developing the disease, and this has fueled studies on the epigenetics of Alzheimer's.

Howard Hu, chair of the SPH Department of Environmental Health Sciences, is the principal investigator on the study. Co-authors include Kelly Bakulski, U-M SPH, and researchers from the U-M Health System and the Department of Veteran's Affairs in Ann Arbor.

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