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Research on advanced Alzheimer's disease investigates novel ways to restore cognitive function

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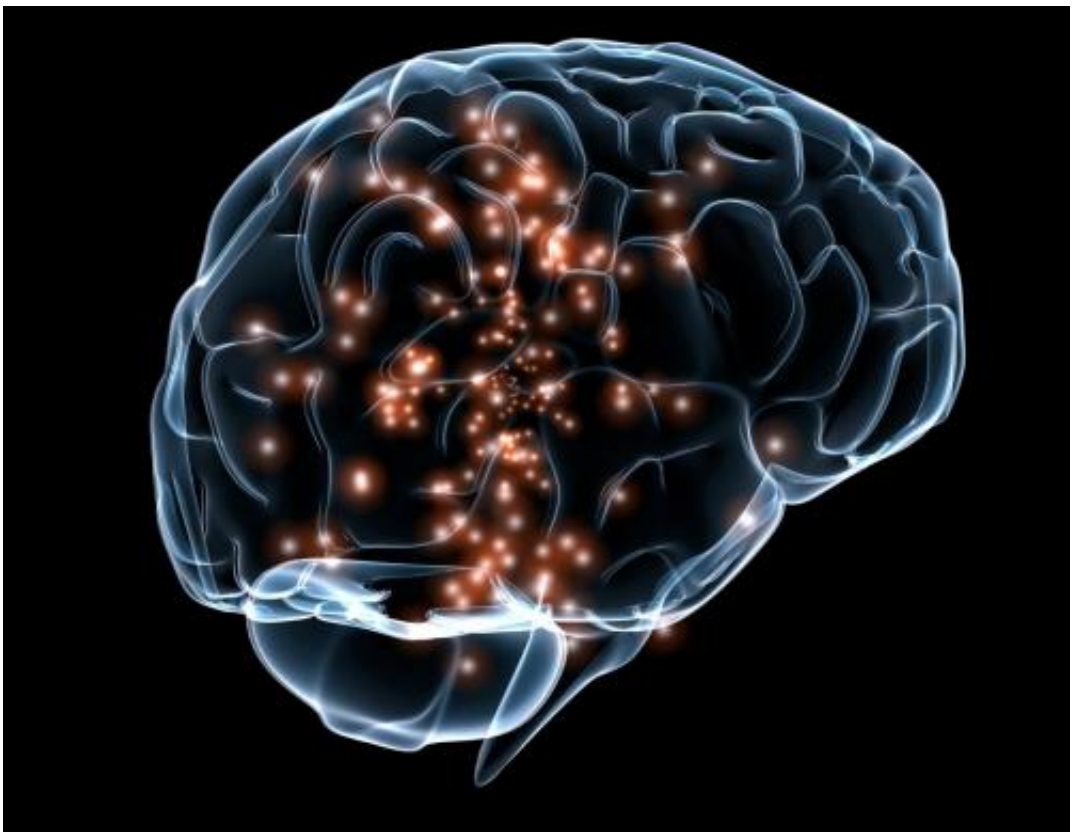

Credit: Wikimedia Commons

While most research on Alzheimer's disease (AD) has focused on early diagnosis and treatment, University at Buffalo scientists are studying genetic and epigenetic factors with the ultimate goal of restoring

function to patients in the later stages of the disease.

The UB team's research will include studies in mouse models carrying gene mutations for familial AD (where more than one member of a family has the disease) and in human stem cell-derived neurons from AD patients.

Zhen Yan, PhD, principal investigator, and Jian Feng, PhD, co-investigator, both professors in the Department of Physiology and Biophysics in the Jacobs School of Medicine and Biomedical Sciences at UB, have received a five-year, $2 million grant from the National Institutes of Health to conduct preclinical research to tease out genetic and epigenetic factors that cause Alzheimer's disease. Epigenetic factors can change gene expression by altering the way that gene promoters, which initiate the copying of genetic information known as transcription, access the cellular machinery that conducts transcription. Such changes may profoundly impact human health.

"We hypothesize that Alzheimer's is produced by a combination of genetic risk factors and environmental factors, such as aging," said Yan, "that induce the dysregulation of specific epigenetic processes that, in turn, lead to impaired cognition."

The UB research will explore how epigenetic changes that accompany Alzheimer's disease also might help identify a much sought-after biomarker for the disease, which could, in turn, allow for novel treatment.

Numerous clinical trials in recent years have focused on reducing amyloid beta plaque in the brain. So far, such efforts haven't yet translated into improving cognitive function, Yan said.

"Our research, by contrast, will target synaptic function, which is at the

root of cognitive function," she explained. "The idea is that this approach will have a more fundamental effect."

She and her colleagues will investigate aberrant histone methylation, an epigenetic process that affects the expression of genes encoding key proteins that allow for signals to be transmitted between neurons.

When this process is dysregulated in Alzheimer's disease, neuronal signaling doesn't function properly, leading to cognitive impairment.

As those with loved ones with Alzheimer's know, even though the patient can easily remember something that happened 20 years ago, the later stages are characterized by a growing inability to recall recently learned information. That kind of short-term memory, Yan explained, is dependent on excitatory transmission in the frontal cortex, mediated by glutamate receptors.

"At the later stages of the disease, we know that there is a loss of glutamate receptors that are crucial for learning and memory," she said. "When these receptors lose the ability to communicate, there is a loss of cognition. Our research will try to restore gene expression in these glutamate receptors using epigenetic tools, with the ultimate goal of restoring cognitive function."

Provided by University at Buffalo