Scientists discover new mechanism that may be important for learning and memory

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(Medical Xpress) -- New findings in mice suggest that the timing when the neurotransmitter acetylcholine is released in the brain's hippocampus may play a key role in regulating the strength of nerve cell connections, called synapses. Understanding the complex nature of neuronal signaling at synapses could lead to better understanding of learning and memory, and novel treatments for relevant disorders, such as Alzheimer's disease and schizophrenia.

Neurons in the hippocampus, one of the parts of the brain that is thought to have a critical function in learning and memory, communicate with each other at synapses by releasing various neurotransmitters, including acetylcholine and glutamate, which stimulate electrical signals in the adjacent neurons.

For years, neuroscientists have been working to determine which cellular processes allow humans to learn from experience and store memories, and how these processes are compromised by conditions such as schizophrenia and Alzheimer's disease. Now, researchers from the National Institute of Environmental Health Sciences (NIEHS), which is part of the National Institutes of Health, believe they have found one such mechanism for synchronizing changes in the strength of synapses. The results of the study will be published online July 13 in the journal *Neuron*.

"We've demonstrated that when we stimulate the release of acetylcholine at just the right time in the hippocampus, we can induce a cellular

change at synapses that use glutamate," said Jerrel Yakel, Ph.D., a senior investigator in the NIEHS Laboratory of Neurobiology and co-author of the paper.

Previous work by other researchers had established that learning and memory is mediated by the strengthening or weakening of synapses, where electrical signals that last less than a hundredth of a second release neurotransmitters that change the electrical impulses of the connected neurons. In this study, Yakel and Zhenglin Gu, Ph.D., a research fellow in Yakel's group and co-author of the publication, used molecular biology techniques to get some of the neurons in mouse brain cells to produce a special light-sensitive protein, and then used a laser to stimulate these neurons to release acetylcholine.

"A change of even a few hundredths of a second in the timing of acetylcholine release can make a difference," said Gu. "No one had shown this was important until now."

Yakel said the findings are also a potentially important step in the study of disorders that affect learning and memory, such as Alzheimer's disease and schizophrenia, where the acetylcholine system and hippocampus are known to play critical roles. For example, amyloid beta peptide is the major component of plaques that form in the brains of Alzheimer's patients and is thought to participate in the memory loss associated with Alzheimer's disease. In this report, Yakel and Gu expand upon earlier findings that amyloid beta peptide disrupts acetylcholine's ability to regulate synaptic strength.

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