# Mechanism in Alzheimer's-related memory loss identified

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Cleveland Clinic researchers have identified a protein in the brain that plays a critical role in the memory loss seen in Alzheimer's patients, according to a study to be published in the journal *Nature Neuroscience* and posted online today.

The protein – Neuroligin-1 (NLGN1) – is known to be involved in memory formation; this is the first time it's been linked to amyloid-associated memory loss.

In Alzheimer's disease, amyloid beta proteins accumulate in the brains of Alzheimer's patients and induce inflammation. This inflammation leads to certain gene modifications that interrupt the functioning of synapses in the brain, leading to memory loss.

Using animal models, Cleveland Clinic researchers have discovered that during this neuroinflammatory process, the epigenetic modification of NLGN1 disrupts the synaptic network in the brain, which is responsible for developing and maintaining memories. Destroying this network can lead to the type of memory loss seen in Alzheimer's patients.

"Alzheimer's is a challenging disease that researchers have been approaching from all angles," said Mohamed Naguib, M.D., the Cleveland Clinic physician who lead the study. "This discovery could provide us with a new approach for preventing and treating Alzheimer's disease."

Previous studies from this group of researchers have also identified a novel compound called MDA7, which can potentially stop the neuroinflammatory process that leads to the modification of NLGN1. Treatment with the compound restored cognition, memory and synaptic plasticity – a key neurological foundation of learning and memory – in an animal model. Significant preliminary work for the first-in-man study has been completed for MDA7 including in-vitro studies and preliminary clinical toxicology and pharmacokinetic work. The Cleveland Clinic plans to initiate Phase I human studies on the safety of this class of compounds in the near future.

Alzheimer's disease is an irreversible, fatal brain disease that slowly destroys memory and thinking skills. About 5 million people in the United States have Alzheimer's disease. With the aging of the population, and without successful treatment, there will be 16 million Americans and 106 million people worldwide with Alzheimer's by 2050, according to the 2011 Alzheimer's Disease Facts and Figures report from the Alzheimer's Association.

**More information:** Epigenetic suppression of neuroligin 1 underlies amyloid-induced memory deficiency, DOI: 10.1038/nn.3618

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