Scientists uncover potential mechanism of memory loss in Alzheimer's disease

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Researchers at the Gladstone Institute of Neurological Disease (GIND) and Baylor College of Medicine have discovered a mechanism by which the protein Amyloid-beta(AB) may impair neurological functions in Alzheimer's disease.

AB, which is known to accumulate in the brains of Alzheimer patients, has long been a focus of research into the causes and treatment of the disease. In a study published in the journal Neuron, Gladstone scientists found that A-beta triggers abnormal overexcitation of the very brain networks that are responsible for learning and memory.

"Such abnormal network activity in Alzheimer's patients was thought to be a collateral or secondary event caused by the degeneration of nerve cells," said Jorge J Palop, PhD, Gladstone research scientist and lead author of the study. "But our study suggests that this activity may actually be a primary effect of A-beta and an early determinant of cognitive failure."

The Gladstone team used several genetically engineered mouse models of AD in which memory deficits are triggered by a human gene that causes high levels of A-beta. They discovered that high levels of A-beta induce an insidious type of seizure activity in learning and memory centers that is not accompanied by the usual twitching and jerking movements seen in many forms of epilepsy. In fact, it took sophisticated brain wave recordings in freely behaving mice by electroencephalography (EEG) and telemetry to detect the seizure

activity.

"We were really surprised by these findings because A-beta had previously been suspected to primarily suppress neuronal activity," said Lennart Mucke, MD, GIND director and professor of neurology and neuroscience at the University of California, San Francisco (UCSF), and senior author of the study. "This abnormal brain activity could play an important role in the development of Alzheimer-related cognitive impairments."

Physicians have long recognized that Alzheimer patients have a higher incidence of convulsive seizures than reference populations. The new study indicates that A-beta is to blame for this problem and raises the disconcerting possibility that these patients may also have non-convulsive seizures that could easily escape detection by standard clinical exams. The investigators are eager to test this hypothesis in a planned follow-up study of human subjects.

"Our results have important therapeutic implications, because the prevention and reversal of non-convulsive seizure activity has not yet been a major focus of clinical trials in Alzheimer's disease. Our results suggest that the suppression of this activity might prevent and possibly even reverse cognitive impairments induced by high levels of A-beta," said Dr. Mucke.

Source: Gladstone Institutes