

New Target for Alzheimer's Disease Identified

ScienceDaily (Sep. 21, 2010) — Neurological researchers at Rush University Medical Center have found a new therapeutic target that can potentially lead to a new way to prevent the progression of Alzheimer's disease. The target called neutral sphingomyelinase (N-SMase) is a protein that when activated, can cause a chain of reactions in the cell leading to neuronal death and memory loss.

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Results from the study funded by the National Institutes of Health and the Alzheimer's Association will be published in the Sept. 22 issue of the *Journal of Neuroscience*.

"There are multiple, neurotoxic, disease-causing pathways that converge on the neutral sphingomyelinase that can cause neuronal loss in the brain of an Alzheimer's patient," said Kalipada Pahan, PhD, neurological researcher and lead investigator at Rush. "If we can stop the activation of the neutral sphingomyelinase, we may be able to stop memory loss and the progression of Alzheimer's disease."

In the brain of a patient with Alzheimer's disease, two abnormal structures called plaques and tangles are prime suspects in damaging and killing nerve cells. While neurons die, other brain cells like astroglia and microglia do not die. These cells become activated and glial cell activation plays a key role in the destruction of neurons. However, the molecular mechanisms by which activated glial cells can kill neurons have been poorly understood until now. Beta-amyloid, which is a protein fragment deposited in the brains of patients who have Alzheimer's disease, causes the activation of glial cells. Neuritic plaques are mainly composed of aggregates of beta-amyloid. When healthy

nerve cells in the brain are exposed to beta-amyloid, they exhibit a number of pathological changes that are characteristic of Alzheimer's pathology.

Researchers at Rush were able to determine that the neutral sphingomyelinase is triggered by the activated brain cells and beta-amyloid. However, when the neutral sphingomyelinase was inhibited by using a small molecule inhibitor and a chemical inhibitor, the activated brain cells and beta amyloid were unable to kill neurons.

Experts tested the two inhibitors using human brain cells in a mouse model and a cell culture model.

"Understanding how the disease process works is important in identifying effective approaches to protect the brain and stop the progression of Alzheimer's disease," said Pahan. "The results of this study are very promising and our next step is to translate these findings to the clinic."

"If we can develop and test a clinical medication that can target the neutral sphingomyelinase, we may be able to halt memory loss in Alzheimer's disease patients," said Pahan.

Alzheimer's disease is an irreversible, progressive brain disease that slowly destroys memory and thinking skills, and eventually even the ability to carry out the simplest tasks. In most people with Alzheimer's, symptoms first appear after age 60. Alzheimer's disease is the most common cause of dementia among older people. Alzheimer's disease affects as many as 5.3 million Americans.

Kalipada Pahan, PhD, is the Floyd Davis Professor of Neurology at Rush University Medical Center.

<http://www.sciencedaily.com/releases/2010/09/100921171347.htm>

As people get older their memory naturally declines and they may forget little things such as not immediately remembering which day of the week it is, occasionally forgetting which word to use or losing things from time to time. You may have started to notice such changes in someone you know and are concerned that something isn't quite right, but you aren't sure what or how serious things are.

You are not alone. Recognising Alzheimer's disease is often difficult, particularly in the early stages. Becoming forgetful does not necessarily indicate Alzheimer's disease, as memory loss can be an effect of ageing. Yet, there are key differences between early Alzheimer's disease symptoms and normal ageing.

People with Alzheimer's disease may know something isn't quite right, but they may not know what. Some people with Alzheimer's disease may hide their deficiencies by following established routines at home or avoiding activities that have become difficult for them.

It is important to recognise the early signs of potential Alzheimer's disease and take action as soon as possible. Alzheimer's disease is typically classified as mild, moderate or severe, with symptoms becoming worse over time. It is most commonly diagnosed when it is more advanced and many people start discussing their concerns with doctors when the person close to them is already

experiencing moderate symptoms. Yet, if Alzheimer's disease is diagnosed early enough, there are things that can be done to help people prepare for the future by managing the disease early on.

Although during normal ageing, people tend to forget things, they are nevertheless aware of this. They remain independent, yet keep in contact with friends and family. They are proficient at using household appliances and do not get lost in familiar surroundings. Alzheimer's disease, however, has specific symptoms that can cause particular problems, not least because people may not be aware they are affected.

People in the early stages of Alzheimer's disease may experience lapses of memory and have problems finding the right words. They may become confused and frequently forget the names of people, places, appointments and recent events. They may feel scared and frustrated by their increasing memory loss. As the disease progresses, people with Alzheimer's disease will need more support from those who care for them. Eventually, they will need help with all their daily activities.

The table below describes what a person possibly affected by Alzheimer's disease is experiencing.

This table is based on information from the Alzheimer's Association

Signs of Alzheimer's disease	Typical age-related changes
Poor judgment and decision-making	Making a bad decision once in a while
Inability to manage a budget	Missing a monthly payment
Losing track of the date or the season	Forgetting which day it is and remembering later
Difficulty having a conversation	Sometimes forgetting which word to use
Misplacing things and being unable to retrace steps to find them	Losing things from time to time

Many other medical problems cause symptoms similar to Alzheimer's disease. That's why it's so important to consult a doctor if you've noticed memory lapses or uncharacteristic mood swings in yourself or in someone close to you.

5 million Americans have Alzheimer's disease and it's currently incurable

Alzheimer's disrupts the communication between your brain's neurons. It causes a protein buildup of plaque, which causes tangled bundles that interfere with your neuronal network's ability to communicate and function properly.