

Alzheimer's discovery could bring early diagnosis, treatment closer

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(PhysOrg.com) -- A discovery made by researchers at McGill University and the affiliated Lady Davis Research Institute for Medical Research at Montreal's Jewish General Hospital offers new hope for the early diagnosis and treatment of Alzheimer's disease.

In a study published in the [Journal of Biological Chemistry](#) on May 15, Dr. Hemant Paudel, his PhD student Dong Han and postdoctoral fellows Hamid Qureshi and Yifan Lu, report that the addition of a single phosphate to an amino acid in a key brain protein is a principal cause of Alzheimer's. Identifying this phosphate, one of up to two-dozen such molecules, could make earlier diagnosis of Alzheimer's possible and might, in the longer term, lead to the development of drugs to block its onset.

The crucial protein, called a [tau protein](#), is a normal part of the brain and [central nervous system](#). But in Alzheimer's patients, tau proteins go out of control and form tangles that, along with senile plaques, are the primary cause of the degenerative disease.

Several years ago, it was discovered that tau proteins in normal brains contain only three to four attached phosphates, while abnormal tau in Alzheimer's patients have anywhere from 21 to 25 additional phosphates.

Paudel and his team have discovered that it is the addition of a single phosphate to the Ser202 amino acid within the tau brain protein that is

the principal culprit responsible for Alzheimer's.

"The impact of this study is twofold," said Paudel, associate professor at McGill's Dept. of Neurology and Neurosurgery, and Project Director at the Bloomfield Centre for Research in Aging at the Lady Davis. "We can now do brain imaging at the earliest stages of the disease. We don't have to look for many different tau phosphates, just this single phosphate. The possibility of early diagnosis now exists.

"Second, the enzyme which puts this phosphate on the tau can be targeted by drugs, so therapies can be developed. This discovery gives us, for the first time, a clear direction towards the early diagnosis and treatment of Alzheimer's."

Paudel and his students worked for years to exclude the phosphates not directly responsible for causing Alzheimer's symptoms. They finally succeeded by working with FTDP-17, a genetic disease with symptoms similar to Alzheimer's, but transmitted via mutations. By genetically manipulating these mutations, they were able to prove that the phosphate on Ser202 almost single-handedly is responsible for the tau abnormalities that cause both FTDP-17 and Alzheimer's.

The disease leads to severe mental degeneration and almost-inevitable death, and there is no known cure, nor even a reliable technique for early diagnosis. A patient is diagnosed with advanced Alzheimer's in the United States every 70 seconds, and deaths due to the disease have increased by a staggering 47 per cent since 2000. With the Baby Boomer population aging, those numbers are expected to explode even further in coming decades.

There are more than 5.3 million people with Alzheimer's in the United States, and more than 300,000 in Canada. Every one of those patients faces years of increasing mental incapacity followed by almost certain

death, with no hope of treatment. The U.S. Alzheimer's Association has called the current situation a "crisis."

Source: McGill University ([news](#) : [web](#))

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