Chemical clears Alzheimer's protein and restores memory in mice

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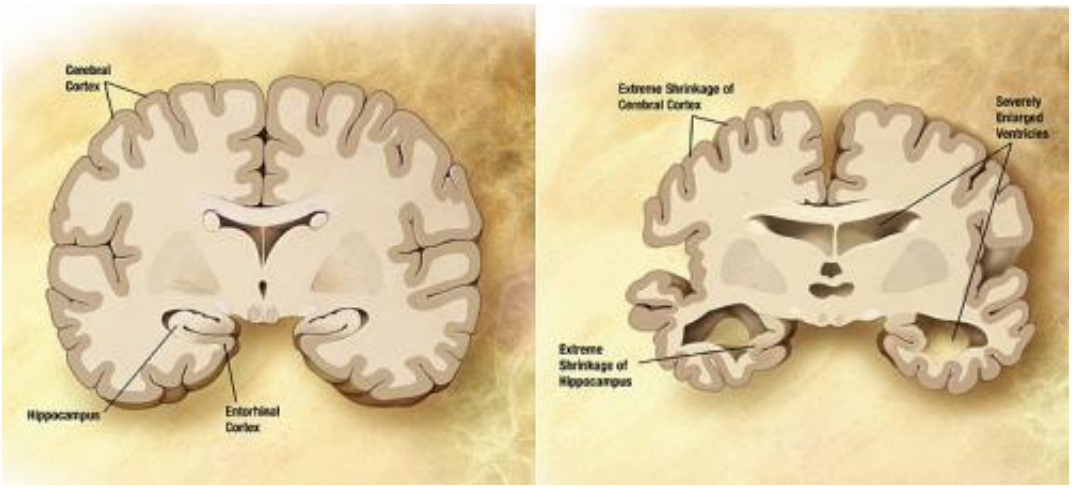

Diagram of the brain of a person with Alzheimer's Disease. Credit: Wikipedia/public domain.

A research team in Korea has tested a chemical in mice genetically altered to develop features of Alzheimer's, showing it can remove a build-up of protein in the brain associated with the disease as well as rescuing memory and behaviour problems in the animals. The findings are published in the journal *Nature Communications* on Tuesday 8 December 2015.

Alzheimer's disease is associated with many abnormal changes in the brain, including the build-up of hallmark proteins amyloid and tau, activation of the immune system and a breakdown in communication

between nerve cells. Amyloid is a protein that is normally present in the brain but behaves abnormally in Alzheimer's, often many years before symptoms show. This abnormal amyloid is sticky and starts to clump together into larger and larger structures – eventually creating large 'plaques' that are visible in the brain under a microscope.

Researchers at the Korea Institute of Science and Technology had previously discovered a set of molecules that could either speed up or slow down the formation of amyloid plaques in test tubes in the laboratory. In this study, they explored the effect of one of these compounds – 4-(2-hydroxyethyl)-1-piperazinepropanesulphonic acid (EPPS) – in mice showing features of Alzheimer's.

In the first experiment, the team found that administering EPPS to mice in drinking water either before, or at the same time as, the mice were injected with abnormal amyloid protein could rescue problems with memory caused by the protein in the brain. The researchers report that EPPS was not toxic to rodents at the doses used and was able to cross into the brain – a particular challenge when developing new drugs for diseases like Alzheimer's.

In a second experiment, the researchers gave EPPS to mice genetically engineered to develop a build-up of amyloid in the brain, to model what is seen in human disease. These mice start to develop amyloid plaques in the brain and show problems with memory and behaviour which get progressively worse over time. In contrast to some other studies, which treat animals before the disease has started to take hold, the researchers waited until the mice had developed large amounts of amyloid plaques in the brain and severe memory problems before treating them with EPPS in drinking water for three months.

The results showed that treatment with EPPS improved the performance of the mice in tests of memory and learning compared to untreated

animals or healthy mice treated with EPPS. Examination of the brains of the mice showed that EPPS had cleared amyloid plaques from the brain and that this difference was greater in animals that had been treated with higher doses of the chemical. Mice treated with EPPS also showed fewer signs of inflammation in the brain.

When the researchers carried out detailed studies of how EPPS was working in laboratory tests, they found evidence that that the chemical could bind directly to clumps of amyloid, breaking them down even at an early stage when they were first starting to stick together.

Dr Simon Ridley, Director of Research at Alzheimer's Research UK, said:

"There is currently a strong focus on developing treatments for Alzheimer's that aim to stop the build-up of the hallmark Alzheimer's protein, amyloid, in the brain. Although some anti-amyloid drugs are currently in late-stage clinical testing, several trials have also failed and there is much debate as whether this is a suitable approach for a new treatment. Many of the current drugs being explored act to stop the formation of amyloid plaques in the brain which mean they may need to be given early in the disease process.

"This interesting study in mice uses a chemical able to break down Alzheimer's plaques in the brain after they've already formed, potentially presenting a way to circumvent the difficult issue of timing with this treatment approach. While this is an appealing prospect, the research is still at the early stage of being explored in animals. Research in animals is an important step in developing any new treatment, but we'll need to see the findings translated into clinical studies in people before we could know the potential of EPPS to treat Alzheimer's in humans.

"With no new treatments for Alzheimer's licensed since 2002, we

urgently need to capitalise on promising early science to make sure it's progressed as quickly as possible towards clinical testing. Alzheimer's Research UK has launched several large initiatives, including our Drug Discovery Alliance, to ensure that positive early findings can be moved towards new treatments for diseases like Alzheimer's more quickly."

Provided by Alzheimer's Research UK