Scientists discover protective molecule against Alzheimer's Disease

April 29 2015

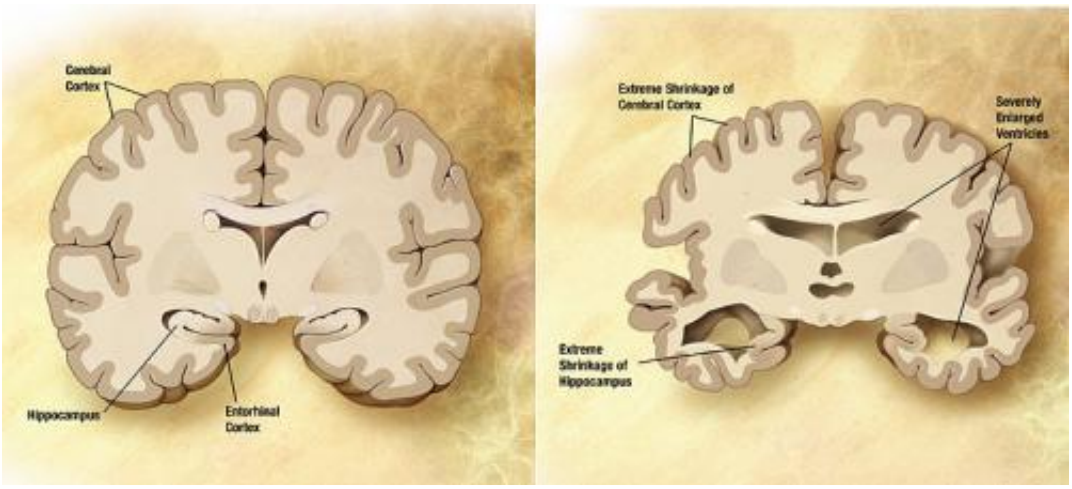

Diagram of the brain of a person with Alzheimer's Disease. Credit: Wikipedia/public domain.

South Australian and Chinese scientists have made a molecular discovery through their research into finding a cure for Alzheimer's Disease.

The research is part of a joint collaboration between groups of scientists led by Professor Xin-Fu Zhou from the University of South Australia and Professor Yanjiang Wang at China's Third Military University.

Earlier this month the research partnership discovered a drug used in the treatment of stroke victims could help stop the progression of the

disease.

The scientists have made a discovery of one of the mechanisms of Alzheimer's Disease.

Professor Xin-Fu Zhou who is the University of South Australia's Research Chair in Neurosciences, says the discovery opens the door to further research into potential treatments.

"Alzheimer's Disease is one of the most devastating diseases currently facing society," Professor Zhou says.

"Its effects are devastating on the individual, their carer and family, and the economic burden on health and aged care systems will only increase without urgent further research."

Currently, there are only a small number of drugs that help with the symptoms of Alzheimer's Disease and there is no cure.

"Alzheimer's Disease is a kind of metabolic disease which produces too much toxic metabolic product and causes breakdown of nerve connectivity," Professor Zhou says.

"Neurodegenerative signals such as amyloid-beta (Aβ) and the precursors of neurotrophins, outbalance neurotrophic signals, causing synaptic dysfunction and neurodegeneration.

"Fortunately, people normally have mechanisms which produce sufficient amounts of nerve protective factors which can prevent the damage of toxic metabolites to the brain.

"The neurotrophin receptor p75 (p75NTR) is a receptor of Aβ and precursors of neutrophins and mediates the toxicity of the

neurodegenerative signals. However, the shedding of its extracellular domain (P75ECD) of p75 from the cell surface is a neuroprotective event and physiologically regulated."

Professors Xin-Fu Zhou and Yanjiang Wang have discovered that with Alzheimer's Disease the neurotrophin receptor p75 which causes nerve damage is increased but the level of neuroprotective p75ECD in the brain and cerebral spinal fluid is reduced to the abnormality in the process of p75ECD shedding.

Their research shows that restoration of p75ECD to the normal level by brain delivery of the gene encoding human p75ECD before or after Aβ deposition in the brains of mice reversed the behavioural deficits and Alzheimer's Disease-type pathologies, such as Aβ deposit, apoptotic (cell death) events, neuroinflammation, Tau phosphorylation, and the loss of dendritic spine, neuronal structures and synaptic proteins. They also showed p75ECD can reduce amyloidogenesis by suppressing β-secretase expression and activities.

"Our data demonstrates that p75ECD is a psysiologically neuroprotective molecule against Aβ toxicity and would be a novel therapeutic target and biomarker for Alzheimer's Disease", Professor Zhou says.

Further studies will be needed in order to validate the research as a drug candidate and diagnostic marker throughout preclinical and clinical trials.

The discovery was published today in *Molecular Psychiatry*.

Provided by University of South Australia