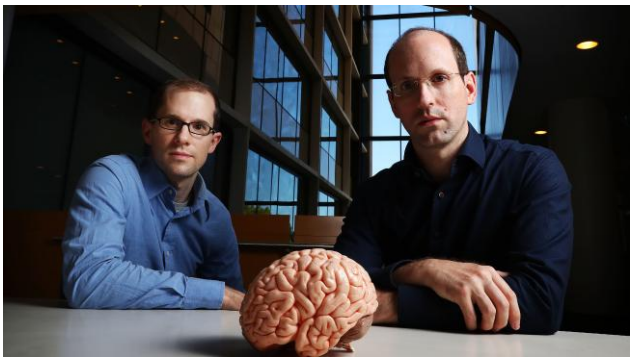
THE AUSTRALIAN

Accused protein exonerated in Alzheimer's trial



Brothers Arne, left, and Lars Ittner say a protein long blamed for causing Alzheimer's disease could be harnessed to fight off the illness. Picture: John Feder

JOHN ROSS THE AUSTRALIAN 6:00AM November 18, 2016

A protein long blamed for causing Alzheimer's disease has been revealed as an unsung hero that tries to fight off the illness.

A study led by two Sydney brothers has overturned scientists' understanding of how Alzheimer's develops in the brain. The research, published in the journal *Science*, could inspire a long-sought way of preventing the main form of dementia — our second-biggest killer, affecting about 400,000 Australians and 47 million people worldwide.

Alzheimer's disease progressively impairs memory, thinking and behaviour. Although its causes are debated, two prime suspects are "plaques" — clusters of protein chunks called amyloid-beta, which accumulate between brain cells — and "tangles" of another protein, tau, which form inside the cells.

Five years ago, Lars Ittner, a German doctor researching brain diseases in Sydney, discovered that the two proteins worked in concert. The theory was that amyloid-beta triggered a change in tau that turned both proteins toxic. However, the new study has found that tau modifies itself in a futile effort to prevent amyloid-beta wreaking havoc. Repeated assaults from the plaque-forming protein eventually strip tau of its protective function, leaving it to form fibrous knots that choke brain cells of vital nutrients.

"This is a completely new mindset," said Professor Ittner, of the University of NSW and Neuroscience Research Australia. "It was the opposite of what we expected."

The study found that yet another protein, p38-gamma, helped tau in its initial efforts to prevent neuron damage, but p38 levels tapered off as Alzheimer's disease

progressed. Experiments in mice found that when p38 was blocked, Alzheimer's-like symptoms emerged. When p38 activity was stimulated, the symptoms disappeared.

The study was co-led by Professor Ittner's brother Arne, a cell biologist who arrived in Sydney in 2010. "We were always thinking of tau as the bad guy," he said. "We had to change our entire concept."