Bath scientists find clues to dementia and Parkinson's

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A research team from our Department of Biology and Biochemistry has found new clues to dementia and Parkinson's disease.

A research team from our Department of Biology and Biochemistry has identified a possible target to reduce the levels of a protein called alpha-synuclein – linked to both Parkinson's disease and dementia with Lewy bodies.

The findings, funded by Alzheimer's Research UK, have been published online this week in the journal *Molecular and Cellular Neuroscience*.

Dementia with Lewy bodies is a type of dementia thought to affect over 100,000 people in the UK, characterised by symptoms of memory loss, fluctuations in attention and alertness, hallucinations, sleep disturbances and movement problems.

Research has already linked changes in the brain in people with dementia with Lewy bodies to those happening in the brain in Parkinson's disease, in which the principal symptoms relate to movement.

To further investigate a common mechanism between the two diseases, Professor David Brown has been investigating a protein called alpha-synuclein.

Professor Brown said: "We know that alpha-synuclein forms abnormal clumps in the brain in dementia with Lewy bodies and in Parkinson's disease. It is thought that one reason for the distinct pattern of symptoms in the two diseases is due to the different parts of the brain affected by these clumps.

"It had been suggested that a related protein, called beta-synuclein, may act to keep alpha-synuclein in check and so we set out to see whether this mechanism could be a target for new treatments."

To do this, the team looked at how both alpha- and beta-synuclein were controlled at a genetic level by studying cells in the laboratory. They discovered that levels of the two proteins appeared to be linked and searched for common factors that could regulate the expression of both inside cells.

The team discovered two factors linked to cell stress that appeared to drive up expression of alpha-synuclein inside cells. They also identified a factor called ZSCAN21 that could drive up expression of beta-synuclein while at the same time, driving down levels of the culprit alpha-synuclein protein.

When they tested the action of ZSCAN21 in cells, they found it reduced the tendency of alpha-synuclein to form its characteristic clumps.

Professor Brown said: "What is particularly exciting is that when we looked at how the levels of these two proteins were regulated at a genetic level, we discovered a common biological mechanism that could tip the balance away from alpha-synuclein.

"Not only does this research provide clues to what could be causing alpha-synuclein to build up in these diseases in the first place, but gives us a target that could potentially stop it from happening."

Dr Simon Ridley, Head of Research at Alzheimer's Research UK, said: "While these experiments are still at an early phase in cells in the laboratory, they reveal an important mechanism to take forward for further investigation. Identifying common pathways involved in multiple diseases, such as alpha-synuclein in dementia with Lewy bodies and Parkinson's disease, has the potential to benefit many people.

"The next step is for the researchers to look in more detail at ZSCAN21 and whether its actions can be harnessed in the design of new treatments for these diseases. We are pleased to have funded this important work, especially in a climate where funding for dementia research is in such short supply."

More information: www.sciencedirect.com/science/ … ii/S1044743113000936

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