

Researchers correct Parkinson's motor symptoms in mice

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A research group led by University of Helsinki Docent Timo Myohanen has succeeded in correcting the motor symptoms associated with Parkinson's disease in mice. Credit: Ville Korhonen

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Parkinson's disease in mice. These results are promising in terms of treatment, since Parkinson's disease is practically always diagnosed only after motor symptoms appear.

Up to two per cent of people over 60 contract Parkinson's. The disease causes severe motor symptoms, as it destroys the nerve cells in the brain's motor areas. The exact cause of the disease is not known, but during the past 15 years research has focused on a protein called alpha-synuclein, which has several functions in the brain areas that regulate motor functions.

This protein is prone to mis-folded forms, which can clump together as aggregates. In Parkinson's disease, aggregated alpha-synuclein proteins accumulate within nerve cells, damaging them. They can also propagate from one cell to the next and spread the impairment of <u>nerve cells</u> in the brain.

Researchers had previously known that the PREP enzyme, which occurs naturally in the body, can increase the formation of such harmful alphasynuclein aggregates in the brain. Now researchers wanted to determine the connection that the enzyme and protein have to the symptoms of Parkinson's disease by blocking PREP in the brain.

In the study, Myöhänen's group set up a mouse model for Parkinson's disease, in which the brain's motor areas were made to produce large amounts of alpha-synuclein. This led to the accumulation of mis-folded proteins in the brains of the mice as expected, resulting in the associated motor symptoms.

PREP blockers restore motor skills

The researchers began treatment with a PREP blocker only when the mice began manifesting clear motor symptoms. The situation would be



similar in a human case of Parkinson's which is typically diagnosed only once the symptoms have appeared. Researchers were astounded by the rapid results.

"After as little as two weeks of treatment, the <u>motor symptoms</u> in the mice had practically disappeared. And they did not reappear until after the experiment was over," explains Myöhänen.

A detailed analysis established that the PREP blocker treatment had stopped the motor areas from becoming further damaged and had cleared the <u>brain</u> of nearly all accumulations of alpha-synuclein.

"We have a long way to go from animal models to human trials, but these results are extremely encouraging in terms of future drug development," says Myöhänen.

The results of Myöhänen's group have been published in the internationally esteemed *Journal of Neuroscience*.

More information: R. Svarcbahs et al. Inhibition of Prolyl Oligopeptidase Restores Spontaneous Motor Behavior in the -Synuclein Virus Vector-Based Parkinson's Disease Mouse Model by Decreasing -Synuclein Oligomeric Species in Mouse Brain, *Journal of Neuroscience* (2016). <u>DOI: 10.1523/JNEUROSCI.2309-16.2016</u>

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