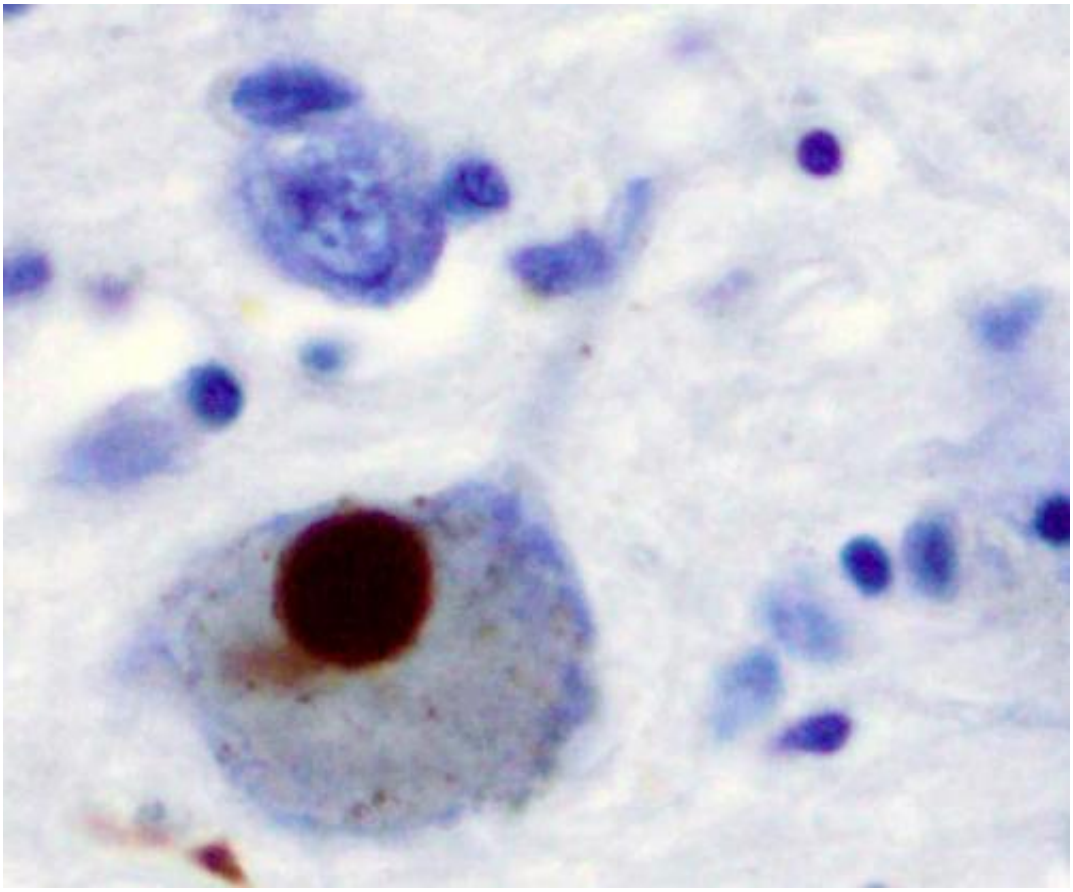
New technique negotiates neuron jungle to target source of Parkinson's disease

September 22 2015



Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneural Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

Researchers from Imperial College London and Newcastle University

believe they have found a potential new way to target cells of the brain affected by Parkinson's disease.

The new technique is relatively non-invasive and has worked to improve symptoms of the disease in rats.

Parkinson's disease causes progressive problems with movement, posture and balance. It is currently treated with drugs, but these have severe side-effects and can become ineffective after around five years. The only treatment subsequently available to patients is deep brain stimulation, a surgical technique where an electrical current is used to stimulate nerve cells in the brain.

As well as being an invasive treatment, it has mixed results - some patients benefit while others experience no improvement or even deteriorate. Researchers believe this is because the treatment is imprecise, stimulating all types of nerve cells, not just the intended target.

The new study, published in the journal *Molecular Neurodegeneration*, examined a less invasive and more precise alternative, designed to target and stimulate a particular type of nerve cell called cholinergic neurons. These are found within a part of the brain called the pedunculopontine nucleus, or PPN.

"If you were to peer inside the PPN, it is like a jungle with a massive variety of nerve cells that behave differently and have different jobs to do," said Dr Ilse Pienaar, Honorary Lecturer in Neuroscience at Imperial College London.

Scientists already suspect that cholinergic neuron cells are involved in Parkinson's disease. This is because in post mortem studies of patients' brains, about half of these cells have perished, for reasons that are

currently unknown.

The researchers worked with rats that had been treated to recreate the symptoms of Parkinson's disease. They used a harmless virus to deliver a specially-designed genetic 'switch' to the cholinergic neurons. The rats were then given a drug that was designed to activate the 'switch' and stimulate the target neurons.

Following the treatment the rats made an almost complete recovery and were able to move normally.

Dr Pienaar adds: "This study confirms that cholinergic neurons are key to the gait problems and postural instability experienced by advanced Parkinson's disease patients. It also suggests that it's possible to target those cells that remain to compensate for those that are no longer functioning effectively, possibly due to weak communication between nerve cells. If we can transfer this technique into people, we believe this could help patients regain mobility."

"At the moment, neurosurgeons are attempting to target specific areas with deep brain stimulation, but it is a blunt tool with correspondingly mixed results. We think we have found a way to target only the cholinergic neurons within an area such as the PPN."

Dr Joanna Elson at the Institute of Genetic Medicine at Newcastle University added: "The structure we studied is complex, very complex. Despite this complexity and the intricacy of the techniques and the brain region analysed, the results are exciting because of the potential to advance patient treatment.

"This paper will help us understand how deep-brain stimulation works, but more importantly it is a step towards offering less invasive treatment options to patients with Parkinson's and other neurodegenerative

disorders."

The researchers believe the technique could transfer into people in the next five to ten years. They also think their technique could have wider potential. Dr Pienaar said: "Parkinson's disease patients experience a complex set of symptoms and we hope to use the same method to understand how different cells within the brain contribute to the disease."

More information: 'Pharmacogenetic stimulation of cholinergic pedunculopontine neurons reverses motor deficits in a rat model of Parkinson's disease' by Ilse S. Pienaar, Sarah E. Gartside, Puneet Sharma, Vincenzo De Paola, Sabine Gretenkord, Dominic Withers, Joanna L. Elson and David T. Dexter is published in *Molecular Neurodegeneration* on 23 September 2015, DOI: 10.1186/s13024-015-0044-5

Provided by Imperial College London

Citation: New technique negotiates neuron jungle to target source of Parkinson's disease (2015, September 22) retrieved 16 April 2023 from https://medicalxpress.com/news/2015-09-technique-neuron-jungle-source-parkinson.html

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