

Are Lewy bodies behind dopamine nerve cell death?



Project information

Lead researcher	Dr Mark Cooper
Location	Institute of Neurology, UCL
Cost	£208,751 over 3 years
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Type of project	Project grant
Project code	G-0910

Project background

Lewy bodies are sticky clumps of protein that are found inside the brains of people with Parkinson's. They form inside nerve cells that produce the chemical dopamine, in a part of the brain that helps control voluntary movement. These dopamine-producing cells begin to die some time after the Lewy bodies appear. And losing these cells gives rise to the movement-related symptoms of Parkinson's, but we don't yet understand the connection between Lewy bodies and the nerve cells dying.

Some facts about Lewy bodies:

- **Alpha-synuclein is a protein that makes up the main part of Lewy bodies.** It's found inside healthy nerve cells too and may be involved in the way that the nerve cells use dopamine. But something happens to change alpha-synuclein in people with Parkinson's and we need to find out more about what.
- **Problems with the gene that produces alpha-synuclein can lead to Parkinson's.** We don't yet know what causes Parkinson's in around 95% of people who get it. But we have learned that alpha-synuclein plays an important part, from research with the small number of people who have inherited specific mutations in the alpha-synuclein gene.

- **Phosphate is a mineral that may play a key role in changing how alpha-synuclein works.** The alpha-synuclein in Lewy bodies has much more phosphate attached to it than it does in healthy cells, on a part of the protein called serine 129. So we need to understand more about how alpha-synuclein usually works, and how adding phosphate to serine 129 changes it.

What the researchers are doing

In this project, Dr Cooper and the UCL team will try to find whether there's a link between the death of dopamine-producing nerve cells and excess phosphate on the serine 129 part of alpha-synuclein. They'll use modern genetic techniques to find out how alpha-synuclein usually affects the way certain nerve cells use dopamine, and whether that changes when phosphate is added to the mix. They also aim to find out why the change from typical to excess levels of phosphate happens.

How the research will help people with Parkinson's

By the end of the project we should know more about how alpha-synuclein affects the way the nerve cells that die in Parkinson's use the chemical dopamine. The work will help us build a picture of why the nerve cells die, together with other projects such as Dr Bazbek Davletov's study at the University of Cambridge. Dr Davletov is looking at how proteins called SNAREs affect alpha-synuclein.

Together, these projects will give us a much better chance of finding the right drug targets for better treatments or a cure for Parkinson's.

For more information, please talk to the Research Team

Call	020 7963 9313
Email	research@parkinsons.org.uk
Write	Parkinson's UK, 215 Vauxhall Bridge Road, London SW1V 1EJ