

The role of the NOS enzyme in Parkinson's



Project information

Lead researcher	Dr Matthew Wood
Location	University of Oxford
Cost	£116,958 over two years
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Type of project	Project grant
Project code	G-0904

Project background

Parkinson's is caused by the loss of nerve cells in part of the brain called the substantia nigra. These cells are responsible for the production of dopamine, a molecule that is involved in the coordination of movement. The death of these cells with a decrease in the levels of dopamine results in the typical symptoms of Parkinson's. In order to find a cure for Parkinson's – to slow down, halt or reverse the death of the nerve cells – we need to understand why they die in the first place. Previous research has shown that there is an inflammation in the brains of people with Parkinson's in the same way, for example, that a person can get an infection. We need to find out how important this inflammation is and whether it could be used as a way of helping to slow down the death of the nerve cells and dampen down some of the symptoms of the Parkinson's.

- **The cells that are responsible for inflammation in the brain are called microglial cells.** They are present in all of our brains, but are not usually active. But when there is some sort of infection, they increase in number, start to work, and produce chemicals that try to deal with what they see as being “foreign” within the brain. This called the inflammatory response, and it is seen in Parkinson's.
- **While we know that inflammation is important,** we don't know whether it may be one of the causes of the death of nerve cells, or whether it may be sparked off when a lot of nerve cells have already died. By examining one of the key factors associated

with inflammation, we will understand its importance and whether using it as a target for drugs may be a useful treatment.

- **One of the key factors produced is nitric oxide.** Nitric oxide (NO) is a chemical produced by the microglial cells when they are sparked off. It is toxic to cells and its role is to get rid of foreign cells, such as bacteria or cells that are no longer working correctly. It is produced by a protein called Nitric Oxide Synthase (NOS). While we know that NO is toxic, we don't really know how important it is in Parkinson's and whether it plays a key role in the death of nerve cells, although there is already some circumstantial evidence that it does.

What the researchers are doing

Dr Wood and his team will use a number of key experimental techniques to look in detail of what NO does in the brain and how it may play a role in Parkinson's. They will do this by changing the amount of the NOS protein in nerve cells. Firstly, they will increase the amount of NO produced by microglial cells grown in a dish and investigate what effect this has on dopamine-producing nerve cells that are grown alongside them. They will then look to see what happens if they turn off NOS in animal models of Parkinson's to see whether this can slow down the death of the nerve cells.

How the research will help people with Parkinson's

If we can understand what happens within the brain when nerve cells die, this may help to provide new ways of developing drugs to slow down, halt or even reverse the process. Understanding the role of inflammation is particularly important, as there are drugs already used for other conditions that block the immune response and which could possibly be used to treat Parkinson's.

For more information, please talk to the Research Team

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