



What Causes Neurodegeneration?

The underlying cause of most neurodegenerative diseases is not fully understood. Only around 5% of cases are a result of genetic mutation (i.e. '**inherited**') therefore the remaining 95% occur randomly (these are called '**sporadic**' cases).

It is well established that neuronal death is the common feature of these diseases and results in many of the symptoms. However the cause of this cell degeneration and death is often not well known.

There is a lot of research currently underway to investigate this and it has been shown that all neurodegenerative diseases feature a build-up of toxic proteins in the brain. In different diseases, the protein itself may vary. The area of the brain it is present in may also differ, but it is believed that the damaging effects to neurons are the same.

Alzheimer's Disease (AD)

This is a common form of dementia which we will explore more in the next activity. There are two known toxic proteins which build up in Alzheimer's. These are called Beta-amyloid and Tau.

Beta-amyloid is chemically 'sticky' and builds up into aggregates called plaques. These plaques can block vital signalling processes from taking place in cells. Tau protein usually helps to support the cells transport system. In AD, tau strands become twisted and build up to forms fibres and 'tangles'. These tangles can no longer support transport, essential nutrients cannot be delivered to neurons and, therefore, they eventually die.

Plaques and tangles have a characteristic spread around the brain (typically starting in the cortex). The further the progression of the tangles and plaques, the worsening of the symptoms of the disease. It can take many years for this process to occur and the rate is very variable between people. Some people may survive up to 20 years however the average survival of an AD sufferer is just 8 years.

Parkinson's Disease

This is a movement disorder, which we will discuss more in activity 4. Here the toxic protein involved is called α -synuclein and this contributes to the death of a particular type of neuron – called dopaminergic neurons.

Dopaminergic neurons usually supply the brain with a chemical called dopamine. Dopamine is responsible for sending messages to the rest of the brain to control movement. Therefore, as dopaminergic cells die, the body becomes less able to co-ordinate and control movement.

Motor Neuron Disease (MND)

As we will explore in activity 5, this is another example of a movement disorder and results from the death of motor neurons. Although there are many differences between MND and



the other forms of neurodegenerative disease we have discussed so far, there is also evidence of a toxic build-up of chemicals and aggregates of proteins in this disease too.

'Oxygen free radicals' are toxic chemicals that are formed as a result of reactions in the body. They can usually be processed and removed from the brain cells before they cause damage. However, in MND this processing and removal is impaired, leading to the damage of motor neurons. Similarly build-up and misfolding of proteins occurs within the neurons and this blocks transport of essential nutrients to other key cells, leading to a cascade of damage.