Huntington's Disease

What is Huntington's Disease?

Huntington's disease is a progressive, incurable and fatal disease of the brain, which was first described by the American physician George Huntington in 1872.

He reported patients who exhibited 'dance like movements' and suggested that the disease may have a hereditary cause. Over 140 years later, after more research, we know Huntington's disease is a rare disease with a worldwide incidence of approximately 3 cases per 100,000 people. The disease is more common in European, American, and Australian populations where prevalence can be as high as 1 in 10 000. However, the estimated number of people with the disease is heavily affected by the stigma associated with the disease, therefore the estimated prevalence is likely to be an underestimation of those who may be affected.

The faulty gene

Huntington's disease is a hereditary disease, as it is passed on from parent to child, however the genetic cause of the disease was only discovered relatively recently in 1993. The genetic nature of Huntington's disease means that if you have the disease there is a 50% chance that you will pass it on to your children. Pre-implantation genetic diagnosis is available for people who know that they carry the gene for Huntington's disease and may want to have children, although this can be expensive, take a long time and there are considerable ethical and moral implications.

Everyone, including you, has the huntingtin gene in our DNA and it is used by our cells as a template to make the huntingtin protein. Scientists are still uncertain about the exact function of the huntingtin protein, but it is thought to be essential in development, cell signalling and cell transport. People with Huntington's disease have a different version of the huntingtin gene, their gene is faulty, as it contains a spelling mistake. The huntingtin gene normally contains a region of DNA with the letters C, A and G repeated, so called CAG repeats, these are the letters that spell out the DNA and read CAGCAGCAGCAGCAGCAG. The unaffected huntingtin gene contains approximately 10 – 35 of these CAG repeats. But , people who are at risk of developing Huntington's disease typically have over 40 CAG repeats within their huntingtin gene, as their gene contains a spelling mistake that means that it contains extra CAG repeats.

The vital discovery of the genetic cause of Huntington's disease has shaped research ever since and led to the creation of a predictive genetic test for the disease. The predictive genetic test can determine if someone has the faulty huntingtin gene and, if so, how many CAG repeats it contains. Although, typically the more CAG repeats a person has, the earlier the disease develops, there is no way of knowing precisely when someone with the faulty gene will begin to develop the symptoms of Huntington's disease. The predictive genetic test for the huntingtin gene can help to inform decisions on family planning, although, many people who are at risk of developing the disease chose not to have the predictive test.

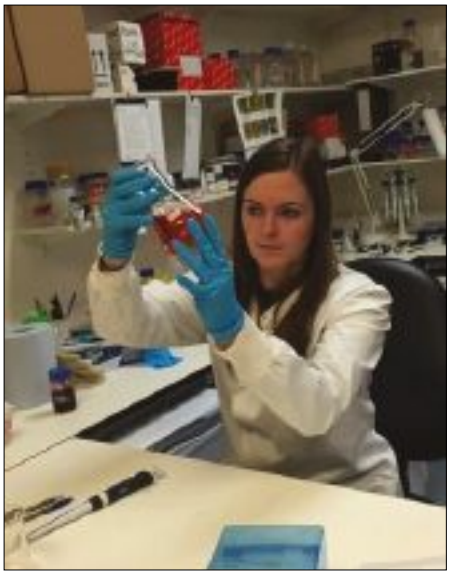
The Symptoms of Huntington's Disease

Huntington's disease has traditionally been known as 'Huntington's chorea', due to the jerking, dance like movements that people with Huntington's disease often have, in the later stages of the disease. Huntington's disease is currently formally diagnosed upon the onset of motor symptoms. However, it is now well known that prior to the development of their uncontrolled movements, people with Huntington's disease may also experience a range of cognitive and psychi-

atric problems. The cognitive and psychiatric symptoms often occur before the motor problems and can significantly impact upon people's lives. For example, people with Huntington's disease can experience depression, mental health problems, delusions and suicidal ideation. Furthermore, increased anxiety, apathy, lack of motivation and sleep disturbances are all common symptoms in the early stages of the disease. Therefore, in addition to the more obvious motor symptoms, the cognitive and psychiatric symptoms of Huntington's disease are important to consider as they can significantly impact upon the lives of people who are living with Huntington's disease.

Animals Models of Huntington's Disease

The discovery of the genetic cause of Huntington's disease led to the creation of a large number of animal models of the disease. By far the most commonly used animal model is the mouse model, due to the relative ease of genetic manipulation. However, other animal models including rats, sheep, pigs and monkeys have all been created with the aim of recapitulating the human disease in an animal model. A huge number of pre-clinical animal models of Huntington's disease are now



Dr. Emma Yhnell at work.

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available in scientific research, these are vitally important in further understanding the disease and in the testing of novel therapeutics.

Treatments and Preventative Measures

There is no cure for Huntington's disease. The current medications available for people with Huntington's disease help to control some of the symptoms of the disease. For example, patients can be prescribed drugs to help with their uncontrolled jerking movements, sleeping problems and depression. However, the medications available are not disease modifying, they may help to control the symptoms, but they will not halt the progression of or prevent the disease.

A large amount of scientific research is currently being conducted to explore possible treatments for Huntington's disease. Non-pharmacological approaches, which often look at life style changes, such as exercise therapies have shown some promise, with patients reporting improved sleeping patterns and quality of life as well as some improvement in disease symptoms. However, exercise therapies can be difficult to implement in a patient population who are lacking in motivation, have sleep disturbances and motor difficulties. A key research interest is that of cognitive training, this approach has worked well in other neurodegenerative diseases and there is evidence from animal studies that cognitive training may help to improve some of the symptoms of Huntington's disease. However, the feasibility and acceptability of conducting cognitive training studies in people with Huntington's disease needs to be explored before further studies of the possible efficacy can be conducted.

Other research has sought to use cell transplantation as a therapy for Huntington's disease. We know that a specific type of cell called medium spiny neurons are lost in Huntington's disease, therefore cell transplantation therapies look to replace these lost cells. The source of cells used in cell transplantation therapies is another key research area. Human foetal tissue is predominantly used in clinical trials of cell transplantation in Huntington's disease. Although, there are a range of logistic, practical and ethical implications of using such tissue. Other studies, utilising animals has explored the use of embryonic stem cells and induced pluripotent stem cells as alternative cells sources for transplantation. However, preliminary evidence of effectiveness and the safety of using such cells needs to be confirmed prior to human studies utilising these cells.

Huntington's disease is a horrible disease which affects whole families. A large amount of research in being conducted to better understand the disease, to help people who are currently living with Huntington's disease and for the future generations of people who will go on to develop it.

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