Lay Summary

BRAIN UK Ref: 23/004

Studying the pathogenesis of Huntington's disease in post-mortem tissues

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Huntington's Disease is a genetic condition that is passed on (inherited) from a person's parents. It is caused by a faulty gene in a person's DNA, where a section of the gene has become repeated, or expanded. This causes brain cells to become damaged over time and stop working. The number of repeats in the gene can be unstable throughout life, and can expand to hundreds, or even thousands of repeats by the time the disease starts, often in one's 30s and 40s.

Recent genetic studies have shown that this repeat expansion is an important factor in when someone will start to show signs of the disease and how the disease will progress. The repeat expansion is caused by DNA repair proteins, which normally try to fix any mistakes in the DNA, but in this case accidently adds additional repeat units, making the expansion bigger. Over time these accumulate into large expansions in vulnerable tissues like the brain, resulting in the death of brain cells.

We would like to measure DNA repair levels and repeat expansion in different tissue regions throughout the body. By doing this we will be able to look at how different amounts of different DNA repair factors affect repeat instability and identify potential targets for future disease modifying medications.

Huntington's Disease is not the only repeat expansion disease and we have previously shown that DNA repair also modifies the onset of these other repeat expansion diseases, so we would like to extend our research to other repeat expansion diseases in the Brain UK collection too.