Clue to cause of motor neurone disease revealed in new genetic study

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Researchers have discovered a fifth genetic mutation associated with typical motor neurone disease, or amyotrophic lateral sclerosis, that has a similar pathological effect to certain genetic mutations revealed in earlier studies. Ultimately, the researchers hope that understanding what is causing motor neurone disease (MND) will lead to new avenues for treatment.

MND is a progressive neurodegenerative disease that attacks the upper and lower motor neurones. Degeneration of the motor neurones leads to weakness and wasting of muscles, causing increasing loss of mobility in the limbs, and difficulties with speech, swallowing and breathing.

The new research, published today in the journal Proceedings of the National Academy of Sciences and led by researchers from Imperial College London, provides strong further genetic evidence that the disease is caused by proteins clumping together in motor neurones, which are the cells that help to control the movement of muscles.

The effect of proteins clumping together in this way, known as protein aggregation, is toxic and it ultimately kills motor neurones. Protein aggregation is believed to be involved in other neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. Previous studies have found a similar association between genetic mutations linked to protein aggregation and MND.

The newly discovered mutation, known as R199W-DAO, has been found in a family with a genetic history of MND. R199W promotes toxic protein aggregation inside motor neurones. It also interferes with levels of D-serine, which modulates the transfer of information between neurones. D-serine accumulates in the spinal cord in people with the sporadic form of MND, suggesting that this plays a role in the disease.

Professor Jackie de Belleroche, the lead author of the study from the Department of Neurosciences and Mental Health at Imperial College London, said: "Motor Neurone Disease is a fatal condition for which there is currently no cure. Our finding is one valuable piece in the puzzle to show what's happening with the disease. Unfortunately we're a long way from finding a cure for MND, but it's only through understanding how MND works that we'll be able to find new ways to treat it."

The researchers discovered the new mutation after looking at 20 members of a family with the genetically inherited form of MND, known as familial MND. Children of a parent with familial MND have a one in two risk of inheriting the disease.

In the study, all of the family members with motor neurone disease had the R199W mutation, whereas none of the individuals with parents unaffected by the disease carried it.

Dr Brian Dickie, director of research development at the Motor Neurone Disease Association, said: "Identifying definitive causes of motor neurone disease (MND), no matter how rare, is of vital importance. It will allow scientists to compare one form of MND with another, to more rapidly identify the common biochemical events that dictate whether a motor neurone lives or dies, no matter what the original cause of the disease is. It serves as a springboard for much greater understanding of MND - and it is through this understanding that effective treatments will be developed."

The researchers did not find the R199W mutation when they looked at a larger population of unrelated people. They looked at the genetic makeup of 1,002 individuals, 780 of whom had no history of motor neurone disease, 23 who had sporadic MND, and 199 who had familial MND, and found no incidences of the mutation.

However, even though this mutation is rare, they

believe that its presence in only those family members with MND means it provides valuable further clues about what is causing the disease.

Provided by Imperial College London