Motor neurone disease: Researchers identify new group of gene suspects

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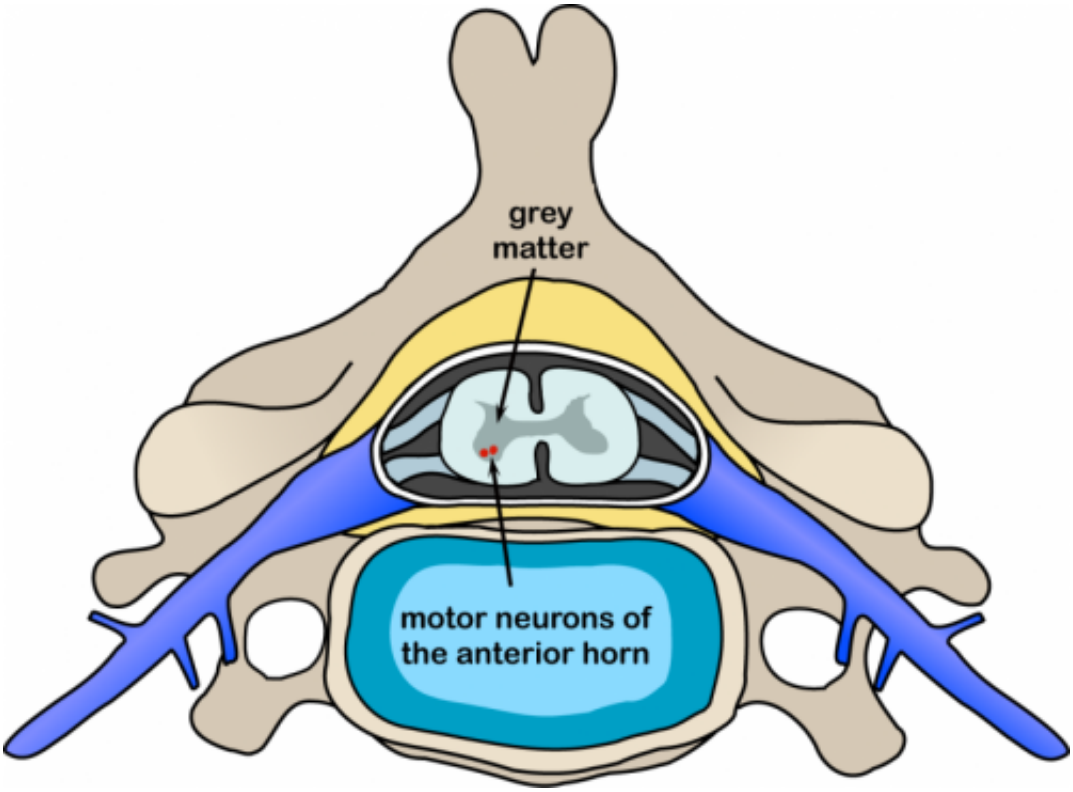

Polio spinal diagram. The poliovirus affects the motor neurons of the anterior horn cells, or the ventral (front) grey matter section in the spinal column, which control movement of the trunk and limb muscles including the intercostal muscles. Credit: Wikipedia/CC BY-SA 3.0

Researchers have identified a new host of gene variants that could make people vulnerable to sporadic motor neurone disease, according to a

report published today in the journal, *Scientific Reports*.

Until recently, it was thought that genetics made little contribution to the disease - also termed amyotrophic lateral sclerosis (ALS) - and that the environment was mostly to blame.

Currently two to three thousand Australians are living with this fatal disease. Motor neurone disease (MND) is a group of diseases in which the nerve cells in the brain and spinal cord controlling the muscles that enable us to move, speak, breathe and swallow slowly degenerate and die.

Death is caused by respiratory failure, which typically occurs within 2 to 5 years of developing this debilitating condition.

MND is also the subject of a major research program at the University of Sydney's Brain and Mind Research Institute. Awareness of MND has spiked in recent times due to the social media campaign supporting the 'Ice Bucket Challenge', and the Oscar winning biopic about cosmologist Stephen Hawking, The Theory of Everything.

"This is an advance in knowledge about the role genetics is likely to play in sporadic forms of motor neurone disease," says the University of Sydney's Associate Professor Roger Pamphlett, a co-author of the new study.

'Sporadic' motor neurone disease accounts for about 90 per cent of cases. It refers to random, isolated cases in which individuals have no known risk factors or family history of the disease.

"The findings indicate that the genetic changes underlying many cases of sporadic motor neurone disease could stem from one of two sources," Associate Professor Pamphlett says. "Sufferers either have a rare

combination of genetic changes they inherited from their otherwise normal parents, or they have newly-arising changes in genes that were not present in their parents."

In an effort to identify genetic variants that may play a role in the disease, the researchers sequenced the protein-coding genes of 44 MND-affected individuals and their parents.

They found that two in five MND-affected individuals had inherited rare, recessive gene variants from their parents, and a quarter had developed novel gene variants that were not present in their parents. The researchers believe these gene variants are "promising candidates" for playing a role in the development of motor neurone disease.

Many of these "genetic suspects" have been identified in other brain-related disease, including Alzheimer's disease, Parkinson's disease and autism. Also, many are involved in biological processes or metabolic pathways implicated in the development of motor neurone disease.

While the researchers cannot yet point to a potential therapeutic application of their findings, identifying genetic changes that underlie MND is the first step in finding ways to manipulate these changes using gene therapy.

Provided by University of Sydney