Scientists discovered genetic cause for rare disorder of motor neurones

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(Medical Xpress)—Scientists have identified an underlying genetic cause for a rare disorder of motor neurones, and believe this may help find causes of other related diseases.

Disorders of motor neurones are a group of progressive neuromuscular disorders that damage the nervous system, causing muscle weakness and wasting. These diseases affect many thousands of people in the UK. A number are inherited but the causes of the majority remain unknown, and there are no cures.

The new study has discovered a gene mutation that causes a rare disorder of motor neurones called distal hereditary motor neuropathy (dHMN). The researchers say their findings raise a possibility that mutations of the same gene or genes with similar roles might underlie other disorders of motor neurones. This could open up the potential for new treatment options, not only for dHMN but also for the wider group of these disorders.

dHMN principally affects muscles of the hands and feet, and sometimes causes a hoarse voice. Symptoms usually begin during adolescence although this can vary from infancy to the mid-thirties.

The study to investigate possible genetic causes of dHMN was led by Professor Andrew Crosby and Dr Meriel McEntagart at St George's, University of London. It has been published in the American Journal of Human Genetics.

The researchers carried out genetic sequencing of 26 members of one family in which 14 members were affected by dHMN and 12 were not. The mutation was found in all the affected members of the family.

The mutation of the gene – called SLC5A7 – was found to disrupt the function of a molecule called the choline transporter (CHT). CHT is responsible for carrying an essential nutrient called choline to the neuromuscular junctions, the areas in the body where nerves meet muscles and that are essential for motor function. This disruption to the function of the neuromuscular junctions leads to the debilitating symptoms.

Mutations of other genes affecting the function of the neuromuscular junctions are known to cause other unrelated neuromuscular disorders. But this is the first time a mutation affecting these specific areas has been linked to any disorder of motor neurones.

Professor Andrew Crosby of St George's, University of London said: "This genetic mechanism has never been linked with a disorder of motor neurones, so it indicates a new biological basis for this group of conditions. Knowledge of the biological pathway related to dHMN will potentially allow us to develop possible treatment options."

Professor Crosby said the latest findings about dHMN will enable them to conduct genetic testing for risk of this rare disease in affected families, using an existing assay. This should also allow them to test for risk of other disorders related to the same genetic mechanism.

"This a very promising step that may provide clues about other unexplained disorders of motor neurones caused by a similar biological disease mechanism", added Professor Crosby.

"A goal now is to investigate this biological mechanism in other patients

with unexplained degenerative disorders of motor neurones."

More information: dx.doi.org/10.1016/j.ajhg.2012.09.019