Genetic testing could be appropriate for all motor neuron disease patients, regardless of family history

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Research from the Sheffield Institute for Translational Neuroscience (SITraN) suggests that routine genetic testing may be appropriate for all MND patients and could impact disease subclassification and clinical care.

The new study, published today (15 February 2021) in the *Journal of Neurology, Neurosurgery and Psychiatry* (*JNNP*), performed targeted genetic sequencing of MND-relevant genes on 100 patients.

Researchers found higher than expected genetic changes in the group of patients. The paper recommends that genetic testing could be appropriate for all MND patients whether or not they have a family history of the disease.

While the majority of MND cases are considered sporadic, five percent to 10 percent have been shown to be familial. Currently only patients with a family history of MND, dementia, or who experience disease onset at a young age are routinely offered genetic screenings in the UK. However, with the development of new therapies targeting specific genetic forms of the disease, researchers are recommending that all MND patients are offered a screening.

Janine Kirby, Professor of Neurogenetics at the University of Sheffield, said "Our study found that 42 percent of patients involved in the screening showed variants in known MND-linked genes. This doesn't mean that 42 percent of MND cases are familial—but shows that some familial and sporadic cases can share the same genetic cause of disease.

"We found that 21 percent of patients had a clinically reportable genetic alteration that has been proven to increase the likelihood of developing MND. Of these, 93 percent had no family history of MND and 15 percent met the inclusion criteria for a current MND gene therapy clinical trial.

"As future studies expand the number of verified genetic causes of MND, we will continue to see if they are also found in cases without a family history ."

Professor Dame Pamela Shaw, Director of SITraN and the NIHR Sheffield Biomedical Research Centre said "Our study suggests that all patients with MND should, with careful counseling, be offered genetic testing."

"We hope that by screening all MND patients for gene mutations that are a known factor in MND, we can further our knowledge on subclassification of the disease, but also ensure that patients have access to clinical trials that are relevant for them personally.

"This is increasingly important in light of the new personalized medicine treatments in development for MND that target a specific gene mutation to ensure that patients have access to potential treatments that could be beneficial to them,"

Dr. Brian Dickie, Director of Research Development at the Motor Neurone Disease Association said "MND is a complex disease involving a complex mix of genetic and environmental factors. This latest research sheds more light on the genetic component and will hopefully lead to greater availability of genetic testing to aid earlier diagnosis and more tailored treatments in the future.

"This study was supported by funds raised through the Ice Bucket Challenge and will be widened to include analysis of additional samples from two other clinics collaborating on this MND Association funded project. This will provide an even clearer picture of the UK MND 'genetic landscape."

MND—also known as amyotrophic lateral sclerosis (ALS) - is an adult-onset neurodegenerative disease characterized by progressive injury and cell death of upper and lower motor neurons. This leads to progressive failure of the neuromuscular system with death, usually from respiratory failure, within 2–5 years of symptoms in most cases.

Currently, there is no cure for MND and no effective treatments to halt or reverse the progression of this devastating disease.

About motor neurone disease (MND):

- MND is a fatal, rapidly progressing disease that affects the brain and spinal cord.
- It attacks the nerves that control movement so muscles no longer work. MND does not usually affect the senses such as sight, sound, feeling etc.
- It can leave people locked in a failing body, unable to move, talk and eventually breathe.
- Over 80% of people with MND will have communication difficulties, including for some, a complete loss of voice.
- It affects people from all communities.
- Around 35% of people with MND experience mild cognitive change, in other words, changes in thinking and behavior. A further 15% of people show signs of frontotemporal dementia which results in more pronounced behavioral change.
- It kills a third of people within a year and more than half within two years of diagnosis.
- A person's lifetime risk of developing MND is around 1 in 300.
- Six people per day are diagnosed with MND in the UK.
- It affects up to 5,000 adults in the UK at any one time.
- It kills six people per day in the UK, this is just under 2,200 per year.
- It has no cure.

More information: Value of systematic genetic screening of patients with amyotrophic lateral sclerosis. *Journal of Neurology, Neurosurgery and Psychiatry* (JNNP)

Provided by University of Sheffield