

# Frequent strenuous exercise increases risk of motor neurone disease

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Frequent strenuous exercise increases the risk of developing (MND) in certain people, new research from the University of Sheffield has found.

The findings, published in the journal *EBioMedicine*, show a causal relationship between [exercise](#) and MND, with [high intensity](#) physical activity likely to contribute to motor neurone injury, but only in individuals with a predisposing genetic profile.

Scientists at the University of Sheffield believe the pioneering study represents a significant step towards unraveling the link between high levels of physical activity and the development of the neurodegenerative condition which affects approximately 5,000 people in the UK.

Over recent years a number of professional sportsmen across the world have shared their experience of living with MND. The condition is commonly referred to as Lou Gehrig's [disease](#) in North America in memory of a professional baseball player for the New York Yankees who developed the condition in his 30's.

The lifetime risk of developing MND is approximately 1 in 400. Previous research has reported an estimated six-times increased risk of MND in professional football players compared to the general population.

Co-author of the study, Dr. Johnathan Cooper-Knock from the University of Sheffield's Neuroscience Institute and Senior Lecturer in Neurology, said: "Complex diseases such as MND are caused by an interaction between genetics and the environment. We urgently need to understand this interaction in order to discover pioneering therapies and preventative strategies for this cruel and debilitating disease.

"We have suspected for some time that exercise was a risk factor for MND, but until now this link was considered controversial. This study confirms that in some people, frequent [strenuous exercise](#) leads to an increase in the risk of MND.

"It is important to stress that we know that most people who undertake vigorous exercise do not develop MND. Sport has a large number of health benefits and most sportsmen and women do not develop MND. The next step is to identify which individuals specifically are at risk of MND if they exercise frequently and intensively; and how much exercise increases that risk."

Senior author of the study, Professor Dame Pamela Shaw Director of the Neuroscience Institute and NIHR Sheffield Biomedical Research Centre at the University of Sheffield, said: "This research goes some way towards unraveling the link between high levels of physical activity and the development of MND in certain genetically at-risk groups. We studied the link using three different approaches and each indicated that regular strenuous exercise is a risk factor associated with MND.

"There are three important key findings of the study. Firstly those who have a genetic make-up favoring strenuous physical activity have an increased risk of developing MND. Many of the 30 plus genes known to predispose to MND change in their levels of expression during intense physical exercise and individuals who have a mutation in the C9ORF72 gene, which accounts for 10 percent of MND cases, have an earlier age of disease onset if they have a lifestyle which includes high levels of strenuous [physical activity](#).

"Clearly most people who undertake strenuous exercise do not develop motor neurone injury and more work is needed to pin-point the precise genetic risk factors involved. The ultimate aim is to identify environmental [risk factors](#) which can predispose to MND, to inform prevention of disease and life-style choices."

MND, or Amyotrophic Lateral Sclerosis (ALS) as it is also known, is a disorder that affects the nerves—motor neurones—in the brain and spinal cord that form the connection between the nervous system and

muscles to enable movement of the body. The messages from these nerves gradually stop reaching the muscles, leading them to weaken, stiffen and eventually waste. The progressive disease affects a person's ability to walk, talk, use their arms and hands, eat and breathe.

Approximately 10 percent of MND cases are inherited, but the remaining 90 percent are caused by complex genetic and environmental interactions which are not well understood—this is known as sporadic MND.

The new research will have a significant impact on the global research effort to identify which individuals based on their genetics are at risk of MND. In time it is hoped that this work will help medical professionals to be able to offer advice to family members of MND patients about the risks so they can make personal decisions about their exercise habits.

Dr. Brian Dickie, Director of Research Development at the Motor Neurone Disease Association said: "In recent years, understanding of the genetics of MND has advanced, but there has been little progress in identifying the environmental and lifestyle factors that increase the risk of developing the disease.

"This is, in part, because the genetic and the environmental studies tend to be carried out in isolation by different research teams, so each is only working with part of the jigsaw. The power of this research from the University of Sheffield comes from bringing these pieces of the puzzle together.

"We need more robust research like this to get us to a point where we really understand all the factors involved in MND to help the search for more targeted treatments."

The Neuroscience Institute at the University of Sheffield brings together

leading experts in medicine, science and engineering to better understand the nervous system and tackle the biggest challenges in neuroscience.

**More information:** Thomas H Julian et al, Physical exercise is a risk factor for amyotrophic lateral sclerosis: Convergent evidence from Mendelian randomisation, transcriptomics and risk genotypes, *EBioMedicine* (2021). [DOI: 10.1016/j.ebiom.2021.103397](https://doi.org/10.1016/j.ebiom.2021.103397)

Provided by University of Sheffield

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