Study identifies protein important for motor coordination and exercise performance

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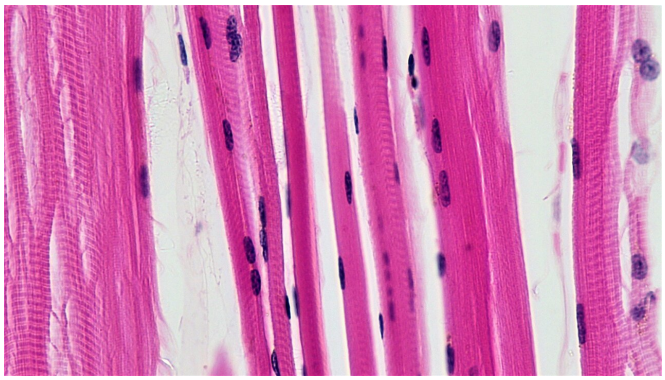

Skeletal muscle fibers. Credit: Berkshire Community College Bioscience Image Library / Public domain

Researchers at Karolinska Institutet in Sweden have identified a protein that improves muscular metabolism, motor coordination and exercise performance in mice. The findings, published in *Cell Metabolism*, could be of therapeutic value for patients with muscle and neurological diseases, such as ALS.

Muscle health is a major determinant of overall health and the best way to keep muscles healthy is to exercise regularly. However, for some patients with debilitating diseases, exercise is not always possible. For that reason, researchers are looking for molecules that can by themselves bring about some of the benefits of physical exercise.

In the current study, researchers at Karolinska Institutet wanted to know how a muscle-produced protein called neurturin affects neuromuscular function. Understanding what signals mediate motor neuron and muscle communication is essential for exploring new treatments for muscle-related and neurological diseases, such as amyotrophic lateral sclerosis (ALS).

"We wanted to know if muscles can talk back to motor neurons by sending their own messages, and to find out what are the consequences of those signals," says Jorge Ruas, professor at the Department of Physiology and Pharmacology, Karolinska Institutet, and corresponding author.

The researchers found that mice that were genetically modified to produce more neurturin in muscle cells significantly improved their muscle metabolism, exercise performance and motor coordination compared to regular mice. The high neurturin mice also had an increased number of motor neurons of a type that is more resistant to degeneration in diseases like ALS.

"To find out that a molecule released from muscle fibers can actually change motor neuron identity, shifting them to a type that is associated with more resistance to degeneration opens really exciting possibilities for the future," Jorge Ruas adds.

As a next step, the researchers are hoping to explore the therapeutic possibilities of neurturin in mouse models of type 2 diabetes, obesity and ALS. They are also working on modifying the administration of neurturin to allow it to be used as a potential drug.

"There's much to be done, but we believe this could be of therapeutic value for patients with metabolic and neuromuscular diseases, such as type 2 diabetes and ALS," says the study's first author Jorge Correia, researcher at the Department of Physiology and Pharmacology, Karolinska Institutet.

The researchers note there were some limitations to the study, including the use of genetic tools and viral vectors to increase the levels of neurturin, which isn't directly applicable from a therapeutic standpoint.

More information: "Muscle-secreted neurturin couples myofiber oxidative metabolism and slow

motor neuron identity", *Cell Metabolism*, DOI: 10.1016/j.cmet.2021.09.003

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