Aerobic exercise could help fight liver diseases, animal study suggests

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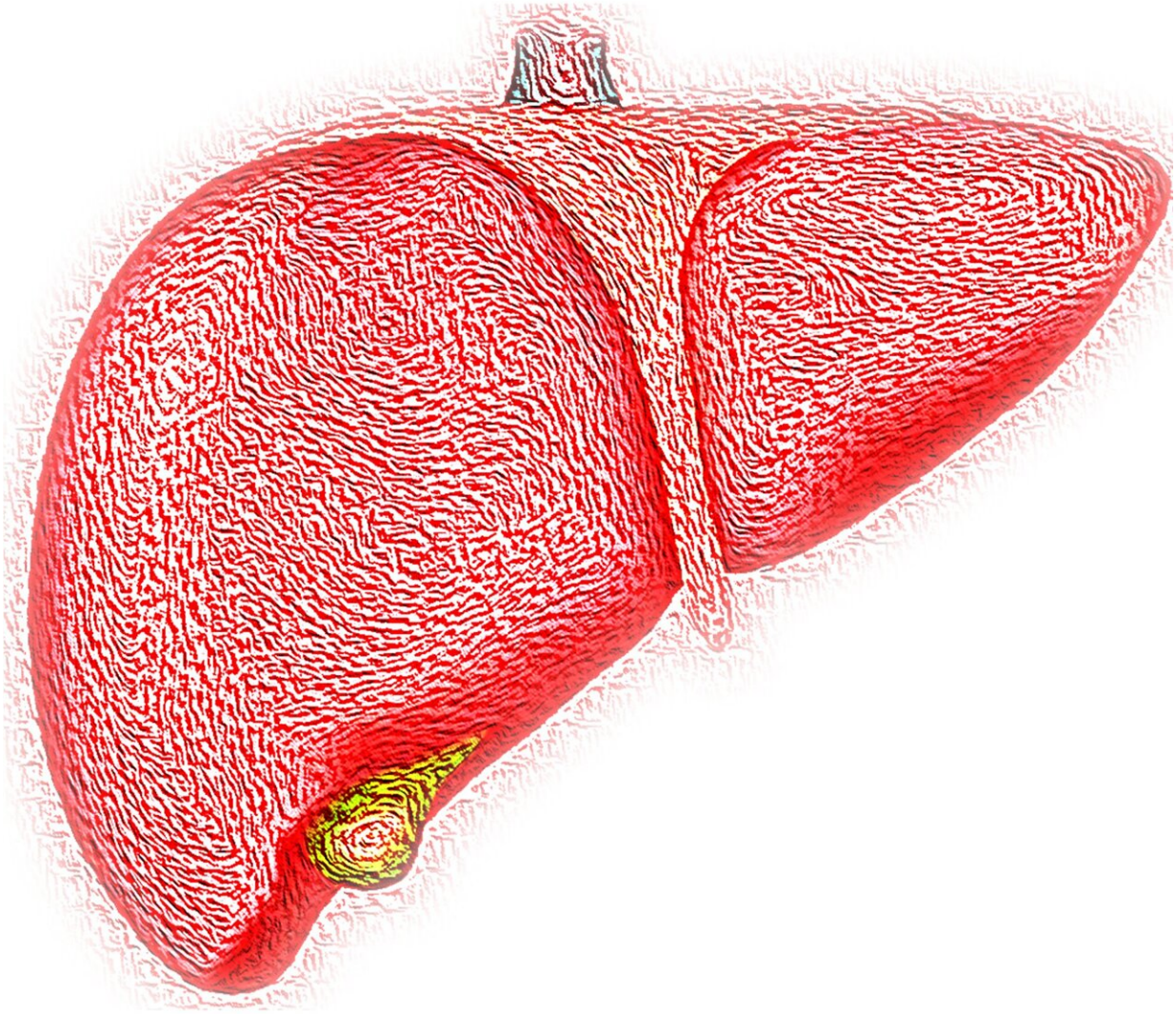

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According to a study conducted on animal models and published in the journal *Metabolism*, aerobic exercise could help fight non-alcoholic fatty liver disease, the most common liver disease worldwide: it affects nearly 24% of the global population and it usually causes a certain stigma among the affected people.

The study opens ways for identifying this process in patients and therefore designing new strategies to prevent its progression.

The article is led by Professor María Isabel Heràndez-Alvarez, from the Faculty of Builogy of the University of Barcelona, the Institute of Biomedicine (IBUB) and the Diabetes and Associated Metabolic Diseases Networking Biomedical Research Center (CIBERDEM), in collaboration with Rodrigo Troncoso, from the University of Chile, and Víctor Cortés from the Pontifical Catholic University of Chile.

When the liver accumulates large amounts of fat

One of the features of fatty liver disease or non-alcoholic steatohepatitis (NAFLD) is the large concentration of lipid droplets (LD) that accumulate in the liver cells.

"Our findings reveal that aerobic exercise, that is, moderate physical activity over time, helps metabolize the fats because it reduces the size of lipid droplets, and therefore, the severity of the disease," notes the author.

"Therefore, the energy demands induced by the exercise determine regulated changes in physical and functional relationships between fat

droplets and mitochondria, the cell organelles that provide energy for the metabolism."

This interaction may take place in a specific population of mitochondria known as peridroplet mitochondria (PDM). "As a result, there is a higher oxidation of lipids in this specific population of mitochondria, a process that helps prevent the progress of the disease."

Discovering a previously unknown connection

"The interaction between the lipid droplets (LD) and the mitochondria is functionally important for the homeostasis of the fat metabolism. Exercise improves fatty liver disease, but to date, it was unknown whether the disease had a direct impact on the interactions between hepatic LDs and mitochondria," notes María Isabel Hernàndez-Alvarez, Ramón y Cajal postdoctoral researcher at the UB's Department of Biochemistry and Molecular Biomedicine.

The study also stresses that mitofusin 2 (Mfn-2)—a protein located in the external membrane of mitochondria—plays a decisive role in this process, since it modifies the communication between lipid droplets and the specific population of mitochondria.

"We found a decrease in the content related to saturated fatty acids in the hepatic mitochondrial membranes of animals that had done physical activity. This suggests that membrane fluidity increases in the mitochondria," notes the researcher.

"In the case of the mice without the Mfn-2 gene, exposed to physical activity, we did not observe changes in the saturation and the metabolism of fatty acids. These results show that the Mfn-2 protein takes part in the regulation of the composition of fatty acids of the mitochondrial membranes in response to exercise."

According to the authors, the Mfn-2 protein would regulate the curve of the mitochondrial membrane in promoting the oxidation of fat in a specific population of mitochondria, through its interaction and ability to form specific domains with membrane phospholipids.

The study is a step forward for boosting research on mediators and molecular mechanisms that could promote new strategies to prevent the progression of NAFLD.

"Considering the Mfn-2 functions in mitochondrial morphology and in the liver, the therapeutic manipulations of the levels and the activity of Mfn-2 could contribute to the improvement of the NAFLD-related inflammation and the fibrosis," concludes the researcher.

More information: Juan Carlos Bórquez et al, Mitofusin-2 induced by exercise modifies lipid droplet-mitochondria communication, promoting fatty acid oxidation in male mice with NAFLD, *Metabolism* (2023). DOI: 10.1016/j.metabol.2023.155765

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