Moderate exercise training improves some of the Marfan syndrome symptoms in mice

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Regular physical activity is a common therapy for people with cardiovascular problems, but not recommended to those with Marfan syndrome, a rare disease of the connective tissue affecting the cardiovascular system. A study conducted jointly by the University of Barcelona and the August Pi i Sunyer Biomedical Research Institute (IDIBAPS) has analysed for the first time this medical recommendation, analysing the impact of exercise in the development of the disease in mice. The results, published in the scientific journal *Journal of the American Heart Association*, show that moderate exercise reduces the progression of aortic aneurysm, one of the most severe symptoms of the disease, which can cause arteries to break.

The study opens the door to studies on humans to verify the positive effects of this kind of exercise in patients with Marfan syndrome.

**Hypothesis without experimental evidence**

Physical activity increases the blood the heart pumps per minute. This increase has an impact on the aorta. "So far, it was thought that this mechanic impact, together with a discrete increase of the arterial pressure, could have negative effects on a weak arteria, like the case of patients with Marfan syndrome, and therefore it would dilate faster if the patient exercised," says Gustavo Egea.

To test this hypothesis, researchers analysed the effects of moderate
exercise on rice with Marfan disease. "During the five months of the experiment, the aorta of those mice who did not exercise dilated twice compared to those mice that were not ill. Mice which exercised experienced a reduction of this dilation until it was indistinguishable from those without the disease," says Eduard Guash. Also, among the beneficial effects, researchers also saw that moderate exercise for five months reduced the size of the heart (cardiac hypertrophy) compared to those mice that did not exercise.

"The new results go against a clinical concept that was accepted without any experimental evidence to prove it: it said that all physical activity increased the risk of speeding up the aneurysm progression" says Gustavo Egea.

**Thinking lifestyle recommendations twice**

Although results in animals should be carefully interpreted before bringing them to patients, researchers highlight that the study provides experimental data that was not available before. "Our work opens the door to conducting studies on humans, but does not verify directly the non-selective recommendation of physical activity to patients with Marfan syndrome," says Gustavo Egea.

Moreover, the researchers note that the study is focused on the impact of moderate exercise, which is the one recommended to people in general and which has been proved to bring cardiovascular benefits. "We did not face the effects of intense and long exercise and we cannot apply our results to other kinds of exercise—other than resistance," says Eduard Guasch.

**Marfan syndrome**
Marfan syndrome is a genetic disease caused by the mutation of a gene that codifies fibrillin I protein, one of the two main compounds of elastic fibers that make up the connective tissue. As a consequence of this mutation, the elastic fiber assembly in tissues is wrong, and therefore the function of relaxation is lost and tissues get damaged faster.

All tissues with elastic fibers or fibrillin I microfibriles are affected, like skin that gets stretch marks, or lungs with emphysema, and the eye lens that moves and causes blindness. The most significant one out of all these dysfunctions is the accelerated weakening of the ascending aorta, which leads to aortic aneurysm and the following dissection and breaking of the aorta.

These clinical manifestations are what is known as Marfan syndrome, which, despite being a minority disease, has a high prevalence of 1/5,000 patients and is hard to diagnose.

People with Marfan are tall with disproportionately large extremities. The average life of non-diagnosed people is around 40 years old, and around 50% of people with this disease are not diagnosed. In Catalonia, there can be around 1,500 people with it. The diagnostic is made with a study of clinical manifestation with a score. When in doubt or verification a genetic analysis can be carried out. Nowadays, the only effective therapeutic solution is surgery, and diagnose and regular monitoring of the aneurysm progression with imaging techniques are essential to increase the life of the patients.

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