A common genetic variant regulates the mental health benefits of exercise

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A new study revealed that a common genetic variant in the brain-derived neurotrophic factor gene reduces the neurobiological benefits induced by physical exercise in mice.

Physical exercise has several beneficial effects on human wellbeing, including anxiolytic and antidepressant effects. However, there are individual differences in response to regular physical exercise. A new study, recently published in *Neuropsychopharmacology*, suggests that these individual variabilities may be accounted for by specific genetic variants.

Researchers from the University of Milan, in collaboration with the Weill Cornell Medical College, reported that physical exercise failed to promote anxiolytic- and antidepressant-like effects in mice genetically engineered to express a human genetic variation in the gene for the brain-derived neurotrophic factor (BDNF).

BDNF is a neurotrophin highly expressed in the adult brain modulating neuronal plasticity. The term neuronal plasticity refers to the capability of brain cells to reorganize pathways and connection throughout life in response to environmental stimuli. A human genetic variant of BDNF, named Val66Met, is carried by approximately 30% of individuals; and some previous studies have shown that this variant is associated with size reduction of specific brain regions and an increased susceptibility to develop neuropsychiatric and neurodegenerative diseases.

The researchers wanted to know how the presence of the BDNF genetic variant could affect the response to physical exercise in mice. To find out, they allowed some groups of mice to voluntarily run on a cage wheel for a month. Behavioral analyses were then performed on mice, showing that physical exercise-induced anxiolytic- and antidepressant-like response was compromised in mutant mice carrying the BDNF genetic variant.

In addition to the behavioral testing, the researchers also performed some molecular analyses finding that, after physical exercise, the levels of BDNF were increased in the hippocampus, a region important for memory and mood regulation, only in wild-type mice but not in mice carrying the BDNF genetic variant.

An important question is how physical exercise may control the expression of certain genes in the brain and their function. Some recent studies have highlighted the importance of specific factors released from the muscle in modulating such responses. Interestingly, the research have found that one of these factors, called FNDC5, normally increased by regular physical exercise in the muscles, was not augmented in the muscles of runner mice carrying the BDNF genetic variant.

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