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Newly-identified exercise gene could help with depression

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Boosting an exercise-related gene in the brain works as a powerful anti-depressant in mice—a finding that could lead to a new anti-depressant drug target, according to a Yale School of Medicine report in *Nature Medicine*.

“The VGF exercise-related gene and target for drug development could be even better than chemical antidepressants because it is already present in the brain,” said Ronald Duman, professor of psychiatry and senior author of the study.

Depression affects 16 percent of the population in the United States, at a related cost of $83 billion each year. Currently available anti-depressants help 65 percent of patients and require weeks to months before the patients experience relief.

Duman said it is known that exercise improves brain function and mental health, and provides protective benefits in the event of a brain injury or disease, but how this all happens in the brain is not well understood. He said the fact that existing medications take so long to work indicates that some neuronal adaptation or plasticity is needed.

He and his colleagues designed a custom microarray that was optimized to show small changes in gene expression, particularly in the brain’s hippocampus, a limbic structure highly sensitive to stress hormones, depression, and anti-depressants.

They then compared the brain activity of sedentary mice to those who were given running wheels. The researchers observed that the mice with wheels within one week were running more than six miles each night. Four independent array analyses of the mice turned up 33 hippocampal exercise-regulated genes—27 of which had never been identified before.

The action of one gene in particular—VGF—was greatly enhanced by exercise. Moreover, administering VGF functioned like a powerful anti-depressant, while blocking VGF inhibited the effects of exercise and induced depressive-like behavior in the mice.

“Identification of VGF provides a mechanism by which exercise produces antidepressant effects,” Duman said. “This information further supports the benefits of exercise and provides a novel target for the development of new antidepressants with a completely different mechanism of action than existing medications.”

Source: Yale University

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