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Tripping the switches on brain growth to treat depression

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Depression takes a substantial toll on brain health. Brain imaging and post-mortem studies provide evidence that the wealth of connections in the brain are reduced in individuals with depression, with the result of impaired functional connections between key brain centers involved in mood regulation. Glial cells are one of the cell types that appear to be particularly reduced when analyzing post-mortem brain tissue from people who had depression. Glial cells support the growth and function of nerve cells and their connections.

Over the past several years, it has become increasingly recognized that antidepressants produce positive effects on brain structure that complement their effects on symptoms of depression. These structural effects of antidepressants appear to depend, in large part, on their ability to raise the levels of growth factors in the brain.

In a new study, Elsayed and colleagues from the Yale University School of Medicine report their findings on a relatively novel growth factor named fibroblast growth factor-2 or FGF2. They found that FGF2 can increase the number of glial cells and block the decrease caused by chronic stress exposure by promoting the generation of new glial cells.

Senior author Dr. Ronald Duman said, "Our study uncovers a new pathway that can be targeted for treating depression. Our research shows that we can increase the production and maintenance of glial cells that are important for supporting neurons, providing an enriched environment for proper neuronal function."

To study whether FGF2 can treat depression, the researchers used rodent models where animals are subjected to various natural stressors, which can trigger behaviors that are similar to those expressed by depressed humans, such as despair and loss of pleasure. FGF2 infusions restored the deficit in glial cell number caused by chronic stress. An underlying molecular mechanism was also identified when the data showed that antidepressants increase glial generation and function via increasing FGF2 signaling.

"Although more research is warranted to explore the contribution of glial cells to the antidepressant effects of FGF2, the results of this study present a fundamental new mechanism that merits attention in the quest to find more efficacious and faster-acting antidepressant drugs," concluded Duman.

"The deeper that science digs into the biology underlying antidepressant action, the more complex it becomes. Yet understanding this complexity increases the power of the science, suggesting reasons for the limitations of antidepressant treatment and pointing to novel approaches to the treatment of depression," commented Dr. John Krystal, Editor of *Biological Psychiatry* and Chairman of the Department of Psychiatry at the Yale University School of Medicine.

More information: The article is "Antidepressant Effects of Fibroblast Growth Factor-2 in Behavioral and Cellular Models of Depression" by Maha Elsayed, Mounira Banasr, Vanja Duric, Neil M. Fournier, Pawel Licznerski, and Ronald S. Duman (doi: 10.1016/j.biopsych.2012.03.003). The article appears in *Biological Psychiatry*, Volume 72, Issue 4 (August 15, 2012)

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