Removing molecule speeds relief from depression

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Getting rid of a protein increases the birth of new nerve cells and shortens the time it takes for antidepressants to take effect, according to an animal study in the March 7 issue of *The Journal of Neuroscience.* The protein, neurofibromin 1, normally helps prevent uncontrolled cell growth. The findings suggest therapeutic strategies aimed at stimulating new nerve cell birth may help treat depression better than current antidepressants that commonly take several weeks to reach full efficacy.

Throughout life, a section of the hippocampus — the brain's learning and memory center — produces new nerve cells. This process, called neurogenesis, is made possible by specialized cells called neural progenitor cells (NPCs). While previous studies show adult neurogenesis declines with age and stress, therapies known to alleviate symptoms of depression, such as exercise and antidepressants, increase neurogenesis.

In the new study, a team of scientists directed by Luis Parada, PhD, of the University of Texas Southwestern, examined neurogenesis after deleting the neurofibromin 1 (Nf1) gene from NPCs in adult mice. Removal of Nf1 increased the number and maturation of newborn nerve cells in the adult hippocampus. Nf1 mutant mice showed reductions in depressive- and anxiety-like behaviors following 7 days of antidepressant treatment, whereas mice without the mutation took longer to show improvements.

"Our findings establish an important role for Nf1 in controlling neurogenesis in the hippocampus and demonstrate that activation of

adult NPCs is enough to regulate depression- and anxiety-like behaviors," said study co-author Renee McKay, PhD, of the University of Texas Southwestern. "Our work is among the first to demonstrate the feasibility of altering mood via direct manipulation of adult neurogenesis," McKay added.

To determine if deleting Nf1 in adult NPCs leads to long-term behavioral changes in mice, the scientists ran 8-month-old mice through a battery of tests designed to measure anxiety- and depressive-like behaviors. Compared with other mice, the mutant mice showed less signs of anxiety and demonstrated resistance to the effects of chronic mild, unpredictable stress. The finding shows even without antidepressants, the deletion of Nf1 from NPCs in adult mice decreases symptoms of depression and anxiety.

"This study demonstrates that inducing neurogenesis is sufficient to produce antidepressant behavioral actions, and provides novel targets for therapeutic interventions," said Ronald Duman, PhD, a neurogenesis expert from Yale University.

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