Researchers find link between neuritin gene activity and stress induced depression

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(Medical Xpress) -- Research teams from the US and Korea have together been studying depression and other mood disorders and have found that chronic stress can block a gene whose job it is to maintain healthy neuron connections in the brain, which in turn can lead to mental ailments. In lab experiments they have found that rats show lowered levels of neuritin gene activity when driven to depression, and that rats with depression tended to do better when given treatment that boosted neuritin activity, suggesting that another means of treating people with mood disorders might be on the horizon. The team has published a paper describing their experiments and results in the *Proceedings of the National Academy of Sciences.*

Prior research has shown that people who suffer from chronic depression tend to lose plasticity, or the ability to organize new information in their brains, specifically in the hippocampus, leading to a degree of atrophy, a condition that makes it difficult for such people to recover from their disorder even when given drugs to help treat the symptoms. Until now however, most drugs that are used to treat mood disorders work by blocking the re-absorption of the brain chemical serotonin. In this new research, the team looked at the role of neuritin gene activity instead.

In lab experiments they first caused rats to become depressed by exposing them to a constantly stressful environment, e.g. putting them alone in a sterile environment, limiting food and alternating their night/day cycle. After about three weeks the rats became lethargic and

unresponsive to normal stimuli. Once that was done, they tested them for the degree of neuritin gene activity, and found that such levels had dropped in all of them. They then treated some of the rates with standard mood stabilizers which helped reduced symptoms as it has in previous research. But then, they treated some of the other rats by infecting them with a virus that causes an increase in neuritin gene activity and found doing so helped the rats just as much as standard therapies and also served to protect their brains from atrophy.

In another experiment the team forced lowered neuritin gene activity in a group of rats but didn't subject them to stress and found the rats became just as depressed as had those in the first experiment.

The team notes that while their results look very promising on paper, assuming the same results would occur with people is premature as there are differences in biology. Their results do however support the notion that stress itself contributes to mood disorders, which is information people can use to help them live more mentally healthy lives right now.

More information: Neuritin produces antidepressant actions and blocks the neuronal and behavioral deficits caused by chronic stress, *PNAS*, Published online before print June 25, 2012, doi: 10.1073/pnas.1201191109

Abstract
Decreased neuronal dendrite branching and plasticity of the hippocampus, a limbic structure implicated in mood disorders, is thought to contribute to the symptoms of depression. However, the mechanisms underlying this effect, as well as the actions of antidepressant treatment, remain poorly characterized. Here, we show that hippocampal expression of neuritin, an activity-dependent gene that regulates neuronal plasticity, is decreased by chronic unpredictable stress (CUS) and that antidepressant treatment reverses this effect. We also show that viral-

mediated expression of neuritin in the hippocampus produces antidepressant actions and prevents the atrophy of dendrites and spines, as well as depressive and anxiety behaviors caused by CUS. Conversely, neuritin knockdown produces depressive-like behaviors, similar to CUS exposure. The ability of neuritin to increase neuroplasticity is confirmed in models of learning and memory. Our results reveal a unique action of neuritin in models of stress and depression, and demonstrate a role for neuroplasticity in antidepressant treatment response and related behaviors.