Medical Xpress

Research identifies gene that changes the brain's response to stress

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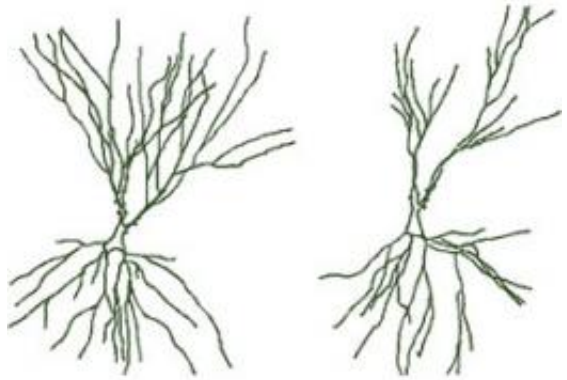

Reduced reach. Tracings of neurons from mice with different levels of BDNF show that a short supply of the protein causes relatively shrunken neurons (right) in some parts of the hippocampus.

(PhysOrg.com) -- Brains change. They change throughout life, responding to developmental but also environmental cues, like stress. Scientists know of several important proteins that play a role in what brains do with new experience. Now they have identified one, brain-derived neurotrophic factor, which must be present at a certain level to enable the brain's "adaptive plasticity," particularly in response to stress.

Stress can literally warp your brain, reshaping some brain structures that help cope with life's pressures. In the short term, the stress response can be helpful — i.e., fight or flight — but over time it leads to a wear and tear that can cause disease in both the brain and other parts of the body.

Digging deeper into what underlies these potentially harmful changes, new research has identified a key protein involved in remodeling the brain under stress. Experiments have found that the brains of mice with an inadequate amount of this protein, called brain-derived neurotrophic factor (BDNF), look similar to those of normal mice that have been under stress for long periods.

The experiments homed in on the gene for a protein that, among other things, enhances the adaptability of neurons in the hippocampus, a brain region that plays a key role in mood, cognition and memory. When normal mice are exposed to chronic stress (simulated by confinement in a wire mesh restraint), there is a significant retraction in the projections, or dendrites, of some of the neurons in the hippocampus, which shrinks in overall volume as well. The new experiments, reported recently in *Hippocampus*, looked at mice that had only one instead of the usual two copies of the gene that produces BDNF. The researchers, from Rockefeller University and Weill Cornell Medical College, found that these mice had brains resembling those of normal mice after extended stress. In other words, stress did not have any effect on the experimental mice.

“The findings suggest that BDNF is one of the proteins that play a role in mediating the brain’s plasticity,” says Bruce S. McEwen, head of Rockefeller’s Harold and Margaret Milliken Hatch Laboratory of Neuroendocrinology.

If researchers can find a way to deplete or supplement BDNF in adult mice, they may be able to answer the question of when in development, or even in adult life, it has the greatest impact. “What we’re seeing is that there may be a developmental window for BDNF’s role, or also that there may be a floor and a ceiling for the right amount of the protein that helps enable adaptive plasticity,” McEwen says.

The new work adds to the understanding of BDNF's interaction with hormones in the brain. McEwen's lab recently discovered that a variant of the BDNF gene is a likely contender for a role in premenstrual disorders, changing mice's performance on certain memory tasks according to their stage of the estrous cycle.

More information: *Hippocampus* online: January 21, 2010. Effect of brain-derived neurotrophic factor haploinsufficiency on stress-induced remodeling of hippocampal neurons, A.M. Magariños, C.J. Li, J. Gal Toth, K.G. Bath, D. Jing, F.S. Lee and B.S. McEwen

Provided by Rockefeller University