Brain chemical reduces anxiety, increases survival of new cells

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New research on a brain chemical involved in development sheds light on why some individuals may be predisposed to anxiety. It also strengthens understanding of cellular processes that may be common to anxiety and depression, and suggests how lifestyle changes may help overcome both.

The animal study, in the May 13 issue of *The* Journal of Neuroscience, shows an important role for fibroblast growth factor 2 (FGF2), a chemical important in brain development, in anxiety. The findings advance understanding of cellular mechanisms involved in anxiety and illuminate the role of neurogenesis, or cell birth and integration in the adult brain, in this process. Together, these findings may offer new drug targets for the treatment of anxiety and potentially for depression as well.

According to the National Institute of Mental Health, approximately 40 million Americans adults have anxiety disorders, and 14.8 million suffer from major depression. These disorders often co-occur: people with anxiety frequently also have depression, and research suggests that the two disorders may share common causes. Previous human studies led by the senior author, Huda Akil, PhD, at the University of Michigan and her collaborators in the Pritzker Consortium, showed that people with severe depression had low levels of FGF2 and other related chemicals. However, it was unclear whether reductions in FGF2 were the cause or effect of the disease.

This new study, led by Javier Perez, PhD, also at the University of Michigan, examined FGF2 levels in rats selectively bred for high or low anxiety for over 19 generations. Consistent with the human depression studies, the researchers found lower FGF2 levels in rats bred for high anxiety compared to those bred for low anxiety.

The study also suggests that environmental enrichment reduces anxiety by altering FGF2. Other researchers have shown that anxiety behaviors in rats can be modified by making changes to their environment, perhaps akin to lifestyle changes for people. Perez and colleagues found that giving the high-anxiety rats a series of new toys reduced anxiety behaviors and increased their levels of FGF2. Furthermore, they found that FGF2 treatment alone reduced anxiety behaviors in the high-anxiety rats.

"We have discovered that FGF2 has two important new roles: it's a genetic vulnerability factor for anxiety and a mediator for how the environment affects different individuals. This is surprising, as FGF2 and related molecules are known primarily for organizing the brain during development and repairing it after injury," Perez said.

Finally, the findings suggest that part of FGF2's role in reducing anxiety may be due to its ability to increase the survival of new cells in a brain region called the hippocampus. Previous research has suggested that depression decreases the production and incorporation of new brain cells, a process called neurogenesis. Although the researchers found that high-anxiety rats produced the same number of new brain cells as low-anxiety rats, they found decreased survival of new brain cells in high-anxiety rats compared to low-anxiety rats. However, FGF2 treatment and environmental enrichment each restored brain cell survival.

"This discovery may pave the way for new, more specific treatments for anxiety that will not be based on sedation — like currently prescribed

drugs — but will instead fight the real cause of the disease," said Pier Vincenzo Piazza, MD, PhD, Director of the Neurocentre Magendie an INSERM/University of Bordeaux institution in France, an expert on the role of neurogenesis in addiction and anxiety who was not involved in the current study.

More information: www.jneurosci.org/

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