MedicalXpress

# Scientists find molecular evidence of brain changes in depressed females

September 16 2011

Researchers at the University of Pittsburgh School of Medicine have discovered molecular-level changes in the brains of women with major depressive disorder that link two hypotheses of the biological mechanisms that lead to the illness. Their results, published online this week in *Molecular Psychiatry*, also allowed them to recreate the changes in a mouse model that could enhance future research on depression.

Although women are twice as likely as men to develop depression and have more severe and frequent symptoms, very little research has focused on them or been conducted in other female animals, noted senior author Etienne Sibille, Ph.D., associate professor of psychiatry, Pitt School of Medicine.

"It seemed to us that if there were molecular changes in the depressed brain, we might be able to better identify them in samples that come from females," he said. "Indeed, our findings give us a better understanding of the biology of this common and often debilitating psychiatric illness."

The researchers examined post-mortem brain tissue samples of 21 women with depression and 21 similar women without a history of depression. Compared to their counterparts, the depressed women had a pattern of reduced expression of certain genes, including the one for brain-derived neurotrophic factor (BDNF), and of genes that are typically present in particular subtypes of brain cells, or neurons, that express the neurotransmitter gamma-aminobutyric acid (GABA.) These

findings were observed in the amygdala, which is a brain region that is involved in sensing and expressing emotion.

In the next part of the project, the researchers tested mice engineered to carry different mutations in the BDNF gene to see its impact on the GABA cells. They found two mutations that led to the same deficit in the GABA subtype and that also mirrored other changes seen in the human depressed brain.

Dr. Sibille noted that researchers have long suspected that low levels of BDNF play a role in the development of depression, and that there also is a hypothesis that reduced GABA function is a key factor.

"Our work ties these two concepts together because we first show that BDNF is indeed low in depression and second that low BDNF can influence specific GABA cells in a way that reproduces the biological profile we have observed in the depressed brain," he said.

The team is continuing to explore the molecular pathway between BDNF and GABA and others that could be important in depression.

Provided by University of Pittsburgh