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Beating the baby blues: A mouse model for postpartum depression

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A new study provides critical insight into the disabling depression experienced by many women during early motherhood. The research, published by Cell Press in the July 31 issue of the journal *Neuron,* reveals new details about the pathogenesis of postpartum depression and provides a mouse model that may lead to development of new treatments for mood disorders associated with pregnancy.

Postpartum depression is a debilitating neuropsychiatric disorder that has been linked with altered levels of steroid hormones in the brain. However, studies designed to mimic hormonal changes during pregnancy only elicit depression in women with a history of postpartum depression, suggesting that hormone fluctuations alone do not trigger this condition. "The pathogenesis of postpartum depression remains unclear, mainly due to the lack of useful animal models to study such a complex disorder," explains lead study author Dr. Istvan Mody from the Department of Neurology at the University of California, Los Angeles.

The GABA neurotransmitter system is associated with anxiety disorders, and GABAA receptors (GABAARs) are a major target of neurosteroid hormones. Although research has revealed that fluctuating hormone levels during the ovarian cycle, pregnancy, and the postpartum period are linked with changes in the GABA system, the functional consequences of these changes are not well understood. Dr. Mody and colleague Dr. Jamie Maguire sought to identify functional changes in GABAARs during pregnancy and the postpartum period in mice and to observe how behavior might be correlated with these changes.

The researchers observed a significant decrease in ? subunit-containing GABAARs during pregnancy, which rebounded immediately postpartum. "As neurosteroid levels increase tremendously during pregnancy, brain mechanisms must have evolved to decrease sensitivity to neurosteroids," offers Dr. Mody. "Rapid return of neurosteroids to prepregnancy levels immediately after birth is normally followed by a commensurate adjustment in the number of GABAARs."

To better understand the behavioral impact of GABAAR ? subunits during pregnancy and postpartum, postpartum behaviors were examined in mice which were deficient in GABAAR ? subunits. The mice, called Gabrd+/? and Gabrd?/?, exhibited depression-like and abnormal maternal behaviors, resulting in decreased pup survival. Importantly, treatment of Gabrd+/? mice with a GABAAR ? subunit-selective agonist to boost GABA activity alleviated abnormal postpartum behaviors and increased pup survival.

The finding that an inability to properly regulate GABAARs during pregnancy and postpartum was associated with depression-like and abnormal maternal behaviors may be highly relevant to the human conditions of postpartum depression. "The Gabrd+/? and Gabrd?/? mouse models will foster further insights into the mechanisms of postpartum depression and may provide much needed therapeutic potential for the large number of new mothers suffering from mood disorders," concludes Dr. Mody.

Source: Cell Press