Treatment of Post-Partum Depression by Altering GABA Receptor Function

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BACKGROUND

Depression during pregnancy and in the postpartum period is an area of much needed research, in terms of both pathophysiology and treatment. Postpartum depression, defined as depression within one year of delivery is very common, affects 10%-22% of adult women. It is found that $GABA_AR$ expression is markedly downregulated by the increase in progesterone derived neurosteroids during pregnancy, an effect which rebounds rapidly in the postpartum period. Neurosteroids are synthesized *de novo* from cholesterol or converted from steroid precursors in the central nervous system. Altered neurosteroid levels are associated with debilitating psychiatric and neurological disorders, including premenstrual dysphoric disorder, premenstrual syndrome, catamenial epilepsy, menstrual migraine, postpartum depression and anxiety. One major impediment to advances in mood disorders research has been a relative lack of animal models of depression, as opposed, for example, to animal models of anxiety disorders or substance abuse. As well, there is a lack of treatments that may reverse postpartum depression and provide mechanistic insight towards development of novel therapeutic agents.

INNOVATION

Previously, UCLA researchers have identified a $GABA_AR$ δ-subunit-selective agonist, THIP (4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol), that may prove to be potential therapeutics for catamenial epilepsy and premenstrual dysphoric disorder (PMDD). Now, researchers report on $GABA_A$ receptor ($GABA_AR$) plasticity during pregnancy and its implications for the pathophysiology of postpartum depression. Researchers have found that THIP also ameliorates the depression-like and abnormal maternal behaviors in mice during pregnancy and postpartum. Therefore, a potential treatment for post-partum depression may be to alter the GABA receptor function through the use of THIP.

In the study, investigators generated a novel mouse model of postpartum depression, $GABA_AR$ δ subunit deficient mouse, which has great potential for evaluating therapeutic interventions. By providing the first mouse model for the disease, further insights into the mechanisms and pathogenesis of postpartum depression can be achieved.

APPLICATIONS

- Potential treatment of postpartum depression through the alteration of GABA receptor function
- Applied pre-clinical research using identified mouse model towards development of new therapies
- Drug discovery for identification of novel small molecule therapeutics targeting $GABA_AR$ δ subunit-containing receptors
- Functional brain imaging studies using magnetic resonance spectroscopy (MRS) and PET imaging

ADVANTAGES

- *In vivo* proof of principle and feasibility for therapeutic intervention has been obtained
- Mechanism of action and target validation has been elucidated
- Research methods and assays have been established

STATE OF DEVELOPMENT

$GABA_AR$ δ subunit deficient mouse are used to provide a working mouse model of postpartum depression.

PATENT STATUS

Patent Pending

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OTHER INFORMATION

CATEGORIZED AS

- **Medical**
  - Research Tools
- **Research Tools**
  - Animal Models

RELATED CASES

2009-042-0

RELATED MATERIALS

- Maguire, J. and Mody, I. GABAAR Plasticity during Pregnancy: Relevance to Postpartum Depression. Neuron, Volume 59, Issue 2, Pages 207-213.

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