A new mouse model of mania

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Bipolar Disorder (BPD or manic-depressive illness) is one of the most serious of all mental disorders, affecting millions of individuals worldwide. Affected individuals alternate between states of deep depression and mania.

While depression is characterized by persistent and long-term sadness or despair, mania is a mental state characterized by great excitement, flight of ideas, a decreased need for sleep, and, sometimes, uncontrollable behavior, hallucinations, or delusions. BPD likely arises from the complex interaction of multiple genes and environmental factors. Unlike some brain diseases, no single gene has been implicated in BPD.

A major limitation to progress in research and treatment has been the lack of an appropriate animal model for BPD. This work was developed to create such a model based on a genetically engineered defect in the GluR6 gene.

The glutamate receptor 6 (GluR6 or GRIK2, one of the kainate receptors) gene resides in a genetic linkage region (6q21) associated with BPD. Kainate receptors respond to the neurotransmitter glutamate, and recent research in mood disorders suggests that the glutamatergic system may play a role in causing mood disorders.

Until now, the role of GluR6 in regulating the mood swings of BPD has been unknown. Furthermore, the gene encoding the GluR6 receptor has recently been linked to treatment emergent suicidal ideation with antidepressants in a pharmacogenetic study. Notably, individuals with

bipolar disorder are most susceptible to antidepressant-induced dysphoric states. In this study, mice of several strains were used to investigate this issue.

Mice who were missing the GluR6 gene were compared with control mice. The mice underwent a series of tests designed to approximate the symptoms of mania. The researchers found that mice that were missing the GluR6 gene exhibited many of these symptoms.

They were more active in multiple tests and super-responsive to amphetamine, which is used in animal models to approximate hyperactivity. These mice also exhibited less anxious or more risk-taking type behavior and less despair-type behavior. They also tended to be more aggressive.

Notably, BPD is most often treated with a class of medications known as mood stabilizers; lithium is perhaps the best known of these medications. The researchers found that chronic treatment with lithium reduced hyperactivity, aggressive displays, and some risk-taking type behavior in mice missing the GluR6 gene.

When biochemical tests were conducted, they also suggested that GluR6 may play a unique role in regulating some of the symptoms of mania. This new animal of mania permits researchers to better understand bipolar disorder and to screen for new treatments that if successful in the animal model can then be translated to the clinic.

Source: Molecular Psychiatry