# Rare Genetic Mutations Linked To Bipolar Disorder

December 21, 2011 |

An international team of scientists, led by researchers at the University of California, San Diego School of Medicine, reports that abnormal sequences of DNA known as rare copy number variants, or CNVs, appear to play a significant role in the risk for early onset bipolar disorder.

The findings will be published in the December 22 issue of the journal *Neuron*.

CNVs are genomic alterations in which there are too few or too many copies of sections of DNA. Researchers have known that spontaneously occurring (*de novo*) CNVs – genetic mutations not inherited from parents – significantly increase the risk for some neuropsychiatric conditions, such as schizophrenia or the autism spectrum disorders. But their role was unclear in bipolar disorder, previously known as manic depression.

Principal investigator Jonathan Sebat, PhD, assistant professor of psychiatry and cellular and molecular medicine at UC San Diego's Institute of Genomic Medicine, and colleagues, found that *de novo* CNVs contribute significant genetic risk in about 5 percent of early onset bipolar disorder, which appears in childhood or early adulthood.

In other words, said the study's first author Dheeraj Malhotra, assistant project scientist in Sebat's lab, "having a *de novo* mutation increases the chances of having an earlier onset of disease."

The cause or causes of bipolar disorder remain unclear. There is a clear genetic component – the disease runs in families – but previous studies that have focused mainly on common inherited variants have met with limited success in identifying key susceptibility genes.

Malhotra said that – while the findings do not conclusively pinpoint a specific gene or genomic region -- the new findings show "convincing" evidence that rare copy number mutations strongly contribute to the development of early onset bipolar disorder. He added that sequencing of complete genomes or exomes of large number of bipolar families is needed to determine the total genetic contribution of all forms of *de novo* mutation to risk for bipolar disorder.

Funding for this research came, in part, from the National Institutes of Health, Ted and Vada Stanley, the Beyster family foundation, Wellcome Trust, Science Foundation Ireland, the Sidney R. Baer, Jr. Foundation and the Essel Foundation.

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