

## A new clue to the genetics of bipolar disorder: Piccolo

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Understanding the genetics of bipolar disorder could lead to new treatments, but identifying specific genetic variations associated with this disorder has been challenging.

A new study in <u>Biological Psychiatry</u> implicates a <u>brain protein</u> called Piccolo in the risk for inheriting bipolar disorder. In the orchestra of neuronal proteins, Piccolo is a member of a protein family that includes another protein called Bassoon. Piccolo is located at the endings of nerve cells, where it contributes to the ability of <u>nerve cells</u> to release their chemical messengers.

Choi and colleagues conducted a creative study to implicate the gene coding for Piccolo (PCLO) in the heritable risk for bipolar disorder.

They compared gene expression patterns in postmortem cortical tissue from people who were diagnosed with bipolar disorder to tissue from people who did not have psychiatric illnesses prior to their death. This analysis identified 45 genes and genetic variations that had significantly altered mRNA levels, and they used this information to narrow the part of the genome that they explored in their genetics study.

They then tested genetic markers (small DNA sequence variations called <u>single nucleotide polymorphisms</u> or SNPs) that are close to the genes that had altered expression levels in the postmortem tissue. A marker for PCLO, SNP rs13438494, emerged as significant in this analysis, suggesting that variation in PCLO contributes to the risk for bipolar



disorder.

"We have taken an innovative approach in correlating gene expression with <u>genetic variation</u> data from well-characterized postmortem brains and then combining with a large scale meta-analysis of genome-wide association studies," explained Dr. Kwang Choi. "If replicated, this study could finally forge a link between gene expression and genome-wide association studies in a complex genetic disorder."

"This study is an example of how better knowledge of brain biology may help to guide our genetics studies," added Dr. John Krystal, Editor of *Biological Psychiatry*.

**More information:** The article is "Gene Expression and Genetic Variation Data Implicate PCLO in Bipolar Disorder" by Kwang H. Choi, Brandon W. Higgs, Jens R. Wendland, Jonathan Song, Francis J. McMahon, and Maree J. Webster. Choi, Song, and Webster are affiliated with the Stanley Laboratory of Brain Research, Rockville, Maryland. Choi is also with the Department of Psychiatry, Uniformed Services University of the Health Sciences, Bethesda, Maryland. Wendland and McMahon are affiliated with the Genetic Basis of Mood and Anxiety Disorders Unit, National Institute of Mental Health, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland. Higgs is from Elashoff Consulting, Redwood City, California. The article appears in Biological Psychiatry, Volume 69, Number 4 (February 15, 2011)

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