

## **Replicating risk genes in bipolar disorder**

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One of the biggest challenges in psychiatric genetics has been to replicate findings across large studies.

Scientists at King's College London, Institute of Psychiatry have now performed one of the largest ever genetic replication studies of bipolar affective disorder, with 28,000 subjects recruited from 36 different research centers. Their findings provide compelling evidence that the chromosome 3p21.1 locus contains a common genetic risk for bipolar disorder, the PBRM1 gene.

The locus at 3p21.1 has also been previously associated with depression and schizophrenia. Using a separate dataset of over 34,000 subjects, they did not confirm association of this same variant with schizophrenia.

Thus, they replicated the association of the marker with bipolar disorder, but not with schizophrenia. This is an interesting finding, in that it distinguishes the heritable risk for bipolar disorder and schizophrenia. It contrasts with the majority of studies that have found that schizophrenia risk genes also contribute to the risk for bipolar disorder.

"This study adds to the recent rapid progress in identifying genes for mental illness. The last few years have seen the identification of about two dozen <u>genetic loci</u> for bipolar disorder and <u>schizophrenia</u>," commented first author Evangelos Vassos. "About half of these are shared between these two disorders, indicating they share some, but not all, <u>genetic causes</u>."



Due to the conflicting results, it is clear that more work is needed to determine the role this locus plays in psychosis, but the evidence seems solid that it is associated with bipolar disorder.

PBRM1, the gene implicated in this study, codes for a protein that is involved in chromatin remodeling or "epigenetics", meaning that it influences the ability of a variety of <u>environmental exposures</u> to influence the expression of a range of genes. It has also been previously implicated in the risk for a form of <u>renal cancer</u>.

"There is growing interest in <u>epigenetic mechanisms</u> that might contribute to the development of bipolar disorder. The implication of a gene involved in chromatin remodeling in bipolar disorder risk adds fuel to this fire," commented Dr. John Krystal, Editor of *Biological Psychiatry*.

Vassos concluded that "future studies may be able to use this information to develop new treatments for these disorders."

**More information:** The article is "Replication Study and Meta-Analysis in European Samples Supports Association of the 3p21.1 Locus with Bipolar Disorder" by Evangelos Vassos, Stacy Steinberg, Sven Cichon, Gerome Breen, Engilbert Sigurdsson, Ole A. Andreassen, Srdjan Djurovic, Gunnar Morken, Maria Grigoroiu-Serbanescu, Carmen C. Diaconu, Piotr M. Czerski, Joanna Hauser, Gulja Babadjanova, Lilia I. Abramova, Thomas W. Mühleisen, Markus M. Nöthen, Marcella Rietschel, Peter McGuffin, David St. Clair, Omar Gustafsson, Ingrid Melle, Olli P.H. Pietiläinen, Mirella Ruggeri, Sarah Tosato, Thomas Werge, Roel A. Ophoff, GROUP Consortium, Dan Rujescu, Anders D. Børglum, Ole Mors, Preben B. Mortensen, Ditte Demontis, Mads V. Hollegaard, Ruud van Winkel, Gunter Kenis, Marc De Hert, János M. Réthelyi, István Bitter, I. Alex Rubino, Vera Golimbet, Lambertus A. Kiemeney, Leonard H. van den Berg, Barbara Franke, Erik G. Jönsson,



Anne Farmer, Hreinn Stefansson, Kari Stefansson, and David A. Collier (doi: 10.1016/j.biopsych.2012.02.040). The article appears in *Biological Psychiatry*, Volume 72 Issue 8 (October 15, 2012)

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