Scientists identify susceptibility factor for bipolar disorder

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A new study provides fascinating insight into the genetic basis of bipolar disorder, a highly heritable mood disorder characterized by recurrent episodes of mania and depression. The research, published by Cell Press online February 24 in the *American Journal of Human Genetics*, identifies a previously unrecognized susceptibility factor for bipolar disorder.

Genome-wide association studies (GWAS) provide a way to systematically sort through all the DNA of many individuals in order to identify genetic variations associated with a particular disease. However, thus far these studies have not been as successful in bipolar disorder as they have been for several other common diseases, such as type II diabetes, Crohn disease, and schizophrenia. Dr. Sven Cichon, from the University of Bonn in Germany, together with his colleagues Dr. Markus M. Nöthen (University of Bonn) and Dr. Marcella Rietschel (Central Institute of Mental Health, Mannheim), led a GWAS and a critical two-step follow-up study of samples from a great number of clinically well-characterized European, American, and Australian individuals with bipolar disorder.

Dr. Cichon and colleagues found that genetic variation in the gene neurocan (NCAN) showed a significant association with bipolar disorder in thousands of patients. Importantly, in a follow up study, these findings were replicated in tens of thousands of individual samples of bipolar disorder. The researchers went on to show that the mouse version of this gene, which is written Ncan and is thought to be involved in neuronal

adhesion and migration, is strongly expressed in brain areas associated with cognition and the regulation of emotions.

Although mice without functional Ncan did not exhibit obvious defects in brain structure or basic cell communication, there did appear to be some perturbation in mechanisms associated with learning and memory, mechanisms that have been associated with the cognitive deficits observed in bipolar disorder. However, the authors caution that Ncan-deficient mice need to be re-examined for more subtle brain changes and behavioral abnormalities.

"Our results provide strong evidence that genetic variation in the gene NCAN is a common risk factor for bipolar disorder," concludes Dr. Cichon. "Further work is needed now to learn more about the biological processes that NCAN is involved in and how NCAN variants disturb neuronal processes in patients with bipolar disorder."

Provided by Cell Press