Bipolar disorder genes, pathways identified

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Neuroscientists at the Indiana University School of Medicine have created the first comprehensive map of genes likely to be involved in bipolar disorder, according to research published online Nov. 21 in the *American Journal of Medical Genetics*.

The researchers combined data from the latest large-scale international gene hunting studies for bipolar disorder with information from their own studies and have identified the best candidate genes for the illness.

The methodology developed at the IU Institute of Psychiatric Research enabled Alexander B. Niculescu III, M.D., Ph.D., and his team to mine the data from the genome-wide association studies and other study results on the levels of gene activity in human blood samples and in animal models. Genes with the highest levels of prominence were determined to be the most active in contributing to the disorder.

The researchers also were able to analyze how these genes work together and created a comprehensive biological model of bipolar disorder.

"Based on our work, we now project that there will be hundreds of genes – possibly as much as 10 percent of the human genome – involved in this illness," said Dr. Niculescu, who is an assistant professor of psychiatry and director of the laboratory of neurophenomics (http://www.neurophenomics.info/) at the IU School of Medicine. "Not all genetic mutations will occur in every individual with bipolar disorder. Different individuals will have different combinations of genetic mutations. This genetic complexity is most likely what made past

attempts to identify genes for the disorder through genetic-only studies so difficult and inconsistent."

Dr. Niculescu compared the process to a Web search. "The process was similar to a Google approach, the more links there are to a page on the Internet, the more likely it is to come up at the top of your search list. The more experimental lines of evidence for a gene, the higher it comes up on your priority list of genes involved in the disorder."

Until now there have been few statistically significant findings in searches of the human genome as it applies to bipolar disorder, he said.

"By integrating the findings of multiple studies, we were able to sort through, identify genes that were most likely to be involved in bipolar disorder, and achieve this major breakthrough in our understanding of the illness," Dr. Niculescu said.

Bipolar disorder, sometimes called manic depression, affects nearly 2.3 million Americans. A serious illness, people who suffer from it can experience mild or dramatic mood swings, shifts in energy and a diminished capacity to function.

Dr. Niculescu, a practicing psychiatrist and a molecular geneticist, said this work opens exciting avenues for psychiatric researchers and clinicians, as well as for patients and their families.

"First and foremost, these studies will lead to a better understanding of bipolar and related disorders," he explained. "Second, the researchers now plan to study individuals to see which combination of genes is present in individuals to come up with a genetic risk score."

The goal, he said, is to be able to apply the risk score to test individuals even before the illness manifests itself for preventive measures –

lifestyle changes, counseling, low-dose medications – or to delay or stop the illness from developing.

"Third, in individuals who already have the illness, genetic testing in combination with blood biomarkers for the disease, could help determine which treatments works best so personalized treatments could be developed," Dr. Niculescu said.

Source: Indiana University