

Bipolar disorder drugs may 'tweak' genes affecting brain

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Study offers clues on causes of condition and how commonly prescribed meds work.

(HealthDay)—Medications taken by people with bipolar disorder may actually be nudging hundreds of genes that direct the brain to behave more normally, according to new research.

The study suggests that [antipsychotic drugs](#) activate a wide range of genes, changing their function, said lead author Dr. Melvin McInnis.

"A gene's activity in any given cell will vary depending on what it's exposed to," said McInnis, a professor of bipolar disorder and depression at the School of Medicine at the University of Michigan.

It's not often that scientists stumble upon something in research that they totally weren't expecting to see. "It was a major surprise to us that people

treated with an antipsychotic [medication] had changes in the [gene expression](#) pattern," McInnis said.

The findings could help point the way to new gene-targeted and stem cell therapies, and provide valuable insight into what causes manic-depressive [mood swings](#), he added.

However, a genetics expert not connected to the study was more cautious about drawing implications from its findings.

Bipolar disorder, also known as manic-depressive illness, affects about 5.7 million American adults, or about 2.6 percent of the U.S. population aged 18 and older, according to the U.S. National Institute of Mental Health (NIMH). The brain disorder causes severe and unusual shifts in mood, energy, activity levels, and the ability to carry out routine daily tasks.

The new research, published in a recent issue of the journal *Bipolar Disorders*, involved examining 26 brains donated to a nonprofit brain bank. Fourteen of the brains were from people who had bipolar disorder. Of those, seven were from people who had been taking one or more antipsychotic medications—such as [clozapine](#), [risperidone](#) and [haloperidol](#)—when they died. Twelve brains were from those with no mental health condition.

In comparing the brains, the scientists observed that the genes of those that had been exposed to antipsychotics at the time of death or during their lifetime were similar to those from people who did not have bipolar disorder. This suggests that the drugs may normalize or suppress the kinds of brain pathology one would expect in bipolar disorder, according to the researchers.

The study also supports the idea that the ability of [brain](#) cells to

effectively communicate with each other may be impaired in people with bipolar disorder. The researchers found that the brains of people who were taking antipsychotics and those who did not have bipolar disorder showed striking similarities in how their brains relayed signals between cell gaps, or synapses, and on high-speed neuronal "freeways" called the nodes of Ranvier.

While antipsychotic medications can often be effective in moderating the effects of bipolar disorder, the side effects are often difficult for people to deal with. These include metabolic syndrome—a combination of symptoms that increase the risk of developing cardiovascular disease and diabetes—as well as weight gain, increased blood sugar levels, and tremors, McInnis said.

However, one expert expressed some concerns about the study.

"It's still not known if these changes just happen to occur or play a key role in the therapeutic effect," said Dr. Francis McMahon, chief of the human genetics branch at the NIMH Intramural Research Program.

McMahon also noted that the researchers don't have data on what medications the brains were exposed to during their lifetimes. "Patients [with bipolar disorder] are exposed to antidepressants, drugs of abuse, and other medications, and we don't have medication exposure data on the brains [of the people without [bipolar disorder](#)]."

For his part, study author McInnis said the research represents a step toward a radical evolution in the design of drugs for psychiatric conditions by the pharmaceutical industry.

"A lot of these psychiatric illnesses fluctuate, but now we give medications at a constant rate, almost as if we were giving a diabetic the same amount of insulin no matter what the person's blood sugar is,"

McInnis said. "Medications as we know them will change based on our understanding of the biological mechanisms behind disease."

More information: Learn more about bipolar disorder from the [U.S. National Library of Medicine](#).

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