

GENETICS

Scientists solve a psychiatric mystery

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A second genetic code that turns our genes on and off works differently in people who suffer from schizophrenia and bipolar disorder, Canadian researchers have discovered.

The finding helps explain a mystery that has puzzled psychiatrists for 50 years. Why, when one identical twin has schizophrenia, does the other have only a 40- to 60-per-cent chance of developing the severe mental illness?

One theory - from the emerging field of epigenetics - is that while their genes are virtually identical, the switches that control them are different. The result is too little or too much of the proteins that make up the brain and keep it running.

Now Arturas Petronis, senior scientist at the Krembil Family Epigenetic Laboratory at the Centre for Addiction and Mental Health in Toronto, has found there is a distinctive pattern in the on-off switches controlling roughly 40 different genes in the brains of psychiatric patients suffering from schizophrenia and bipolar disorder.

The work, published in the American Journal of Human Genetics, lays the groundwork for a new way of understanding psychiatric illnesses. One day it could lead to new ways to treat or diagnose severe mental illnesses.

"Traditionally, when we talk about human diseases we talk about two groups of factors, genetic factors and environmental factors. Now we are bringing in a third layer, which will be equally important if not more important than DNA sequences and environment," Dr. Petronis said.



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He is a pioneer in the field of human epigenetics, the study of genetic changes that don't involve mutations in DNA.

If DNA is the hardware of inheritance, the epigenetic operating system is the software, controlling the 30,000 genes that carry instructions for the proteins that make up our bodies and keep them working.

Scientists are still deciphering what they describe as a second genetic code. They know that a number of chemicals in our bodies act like dimming switches and determine whether every gene in each cell produces a lot of a particular protein, very little or none of it.

In laboratories around the world, researchers are looking at the different ways these dimming switches work.

The process they perhaps understand the best is called methylation, in which chemical tags are added to the DNA in a way that silences, or partially silences, the gene.

Dr. Petronis and his colleagues studied methylation patterns in brain tissue from 100 people.

About a third of the postmortem samples they obtained from a brain bank in the United States came from patients who had suffered from schizophrenia, a third from people who had bipolar disorder and a third from healthy controls, matched for age and sex.

They looked at 12,000 genes and found significant differences in the brains of the patients who suffered from serious mental illnesses.

There were distinct differences in the methylation of 40 genes. Some of the differences were shared between the schizophrenia and bipolar patients, and some were unique to each disease.

Some of the genes are involved in brain development, or the exchange of chemical messages in the brain. Others are mysteries. Dr. Petronis says he has no idea what they do.

Bipolar disorder, which used to be known as manic depression, causes severe shifts in a person's mood, energy and ability to function. It affects an estimated 2.6 per cent of adults. Someone with an identical twin with the disorder has a 60-per-cent chance of getting it.

Schizophrenia is characterized by delusions, hallucinations, disturbances in thinking and withdrawal from social activity. It affects one in 100 Canadians and their families, according to the Schizophrenia Society of Canada.

Epigenetics helps explain why Pamela Spiro Wagner started hearing voices the day John. F. Kennedy was assassinated - she was later diagnosed with schizophrenia - while her identical twin Carolyn Spiro remained healthy. She became a psychiatrist and was on call at a Boston hospital when her sister was admitted in a catatonic state, one arm extended in the air.

"This can't be my twin," she recalls thinking at the time. The two wrote a memoir, published in 2005, called *Divided Minds: Twin Sisters and their Journey Through Schizophrenia*.

But epigenetics could also help explain more than the differences between people who are genetically identical. Scientists are now looking at many common diseases, including cancer, Parkinson's, Alzheimer's and lupus, to see if they might be caused, at least in part, by the switching system that activates and deactivates genes.

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