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Five mental disorders share genetic links, huge study says

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Washington • The largest genetic study of mental illnesses to date finds five major disorders may not look much alike but they share some gene-based risks. The surprising discovery comes in the quest to unravel what causes psychiatric disorders and how to better diagnose and treat them.

The disorders — autism, attention deficit-hyperactivity disorder or ADHD, bipolar disorder, major depressive disorder and schizophrenia — are considered distinct problems. But findings published online Wednesday suggest they're related in some way.

"These disorders that we thought of as quite different may not have such sharp boundaries," said Dr. Jordan Smoller of Massachusetts General Hospital, one of the lead researchers for the international study appearing in *The Lancet*.

That has implications for learning how to diagnose mental illnesses with the same precision that physical illnesses are diagnosed, said Dr. Bruce Cuthbert of the National Institute on Mental Health, which funded the research.

Consider: Just because someone has chest pain doesn't mean it's a heart attack; doctors have a variety of tests to find out. But there's no blood test for schizophrenia or other mental illnesses. Instead, doctors rely on symptoms agreed upon by experts. Learning the genetic underpinnings of mental illnesses is part of one day knowing if someone's symptoms really are schizophrenia and not something a bit different.

"If we really want to diagnose and treat people effectively, we have to get to these more fine-grained understandings of what's actually going wrong biologically," Cuthbert explained.

Added Mass General's Smoller: "We are still in the early stages of understanding what are the causes of mental illnesses, so these are clues."

The Psychiatric Genomics Consortium, a collaboration of researchers in 19 countries, analyzed the genomes of more than 61,000 people, some with one of the five disorders and some without. They found four regions of the genetic code where variation was linked to all five disorders.

Of particular interest are disruptions in two specific genes that regulate the flow of calcium in brain cells, key to how neurons signal each other. That suggests that this change in a basic brain function could be one early pathway that leaves someone vulnerable to developing these disorders, depending on what else goes wrong.

For patients and their families, the research offers no immediate benefit. These disorders are thought to be caused by a complex mix of numerous genes and other risk factors that range from exposures in the womb to the experiences of daily life.

"There may be many paths to each of these illnesses," Smoller cautioned.

But the study offers a lead in the hunt for psychiatric treatments, said NIMH's Cuthbert. Drugs that affect calcium channels in other parts of the body are used for such conditions as high blood pressure, and scientists could explore whether they'd be useful for psychiatric disorders as well.

The findings make sense, as there is some overlap in the symptoms of the different disorders, he said. People with schizophrenia can have some of the same social withdrawal that's so characteristic of autism, for example. Nor is it uncommon for people to be affected by more than one psychiatric disorder.