Brain changes precede schizophrenia and autism

Carriers of high-risk genes show cognitive impairments and could benefit from early intervention.

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In children with certain gene variants, symptoms similar to common learning disabilities could be omens of serious psychiatric conditions.

People who carry high-risk genetic variants for schizophrenia and autism have impairments reminiscent of disorders such as dyslexia, even when they do not yet have a mental illness, a new study has found. The findings offer a window into the brain changes that precede severe mental illness and hold promise for early intervention and even prevention, researchers say.

Rare genetic alterations called copy number variants (CNVs), in which certain segments of the genome have an abnormal number of copies, play an important part in psychiatric disorders: Individuals who carry certain CNVs have a several-fold increased risk of developing schizophrenia or autism[1]. But previous studies were based on individuals who already have a psychiatric disorder, and until now, no one had looked at what effects these CNVs have in the general population. In a study published today in *Nature*[2], researchers report that people with these variants but no diagnosis of autism or a mental illness still show subtle brain changes and impairments in cognitive function.

“In psychiatry we always have the problem that disorders are defined by symptoms that patients experience or tell us about, or that we observe,” says study co-author Andreas Meyer-Lindenberg, a psychiatrist and the director the Central Institute of Mental Health in Mannheim, Germany, affiliated with the University of Heidelberg. This work, on the other hand, provides a glimpse into the biological underpinnings of people who are at risk of psychiatric disorders, he says.

The team searched a genealogical database of more than 100,000 Icelanders, focusing on 26 genetic variants that have been shown to increase the risk of schizophrenia or autism. They found that 1,178 people in the database, or 1.16% of the sample, carried one or more of these CNVs.

Early warning

Meyer-Lindenberg and his colleagues then recruited carriers between the ages of 18 and 65 who had not previously been diagnosed with any of a range of neuropsychiatric disorders. They put these participants and several control groups through a battery of neuropsychiatric and cognitive tests, and used magnetic resonance imaging (MRI) to observe structural brain differences.

People carrying the variants performed worse than controls from the general population on cognitive tests and measures of general day-to-day functioning, and they were more likely to show a history of various learning disabilities. For instance, the researchers found that carriers of one particular CNV, a deletion in a specific region of chromosome 15, tend to have a history of dyslexia and a difficulty in understanding numbers. MRI showed that the same deletion alters brain structure in a way also seen in individuals with early stages of psychosis, and in individuals with dyslexia.

“It’s not as if [the variants] are just one incremental factor in your risk for psychosis and by themselves are not doing much,” says Jonathan Sebat, a human geneticist at the University of California in San Diego who was not involved in the research. “They actually are impacting cognition in a significant way.”

“Now we want to see whether we can find mutations in the genome that affect how people perform on exams in school, how people advance through the educational system, and how they do socio-economically,” says Kári Stefánsson, a co-author of the study and chief executive and co-founder of deCODE Genetics, a biotechnology company based in Reykjavik. “We are going to take this out of the realm of artificial tests into the real world.”

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References

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