

Researchers discover new schizophrenia gene

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Researchers at the Johns Hopkins University School of Medicine are one gene closer to understanding schizophrenia and related disorders.

Reporting in the Jan. 9 issue of the *American Journal of Human Genetics*, the team describes how a variation in the neuregulin 3 gene influences delusions associated with schizophrenia.

"Neuregulin 3 is clearly one more gene to add to the few currently known to contribute to schizophrenia," says David Valle, M.D., director of the McKusick-Nathans Institute of Genetic Medicine at Hopkins.

"There's much more to do, but we're making progress."

Schizophrenia is a varied condition with a number of symptoms not shared by all affected. This could be one reason why it's been difficult to identify genes that contribute to the condition.

To address this, the team first rigorously separated the 73 different symptoms into nine distinct factors associated with the condition—prodromal, negative, delusion, affective, scholastic, adolescent sociability, disorganization, disability, hallucination.

Then, using genetic samples from more than 450 people with schizophrenia and their parents as well as unrelated non-affected people for comparison, the team focused on one region of chromosome 10 that previously had been implicated to contain genes that contribute to the condition. They analyzed more than 1,400 single nucleotide polymorphisms, or SNPs for short, to see if any particular SNPs were more frequently carried by schizophrenia patients than unaffected

people.

They found three SNPs strongly associated with delusions, and all three SNPs are located in the neuregulin 3 gene. In fact, of the team's top 20 most significant SNPs, 13 of them are located at or near this gene, but rather than being associated with delusion, the other SNPs are associated with scholastic, disorganization and hallucination factors.

"Neuregulin 3 makes sense because it's turned on mostly in the central nervous system, and the related gene neuregulin 1 also has been shown to be associated with schizophrenia," says Dimitrios Avramopoulos, M.D., Ph.D., an associate professor of psychiatry and member of the Institute of Genetic Medicine.

"We're still at the stage of trying to understand the disease, figuring out what goes wrong in the brain," says Avramopoulos who adds that the next step for this team is to follow up and sequence the neuregulin 3 gene from a number of the patients in this study to look for rare genetic variants that might also contribute to the condition.

On the web: www.cell.com/AJHG/home

Source: Johns Hopkins Medical Institutions

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