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It's No Delusion: Evolution May Favor Schizophrenia Genes

New research reveals that genes related to the debilitating disorder may also provide developmental advantages

By Nikhil Swaminathan on September 6, 2007

Schizophrenia, the psychotic disorder marked by hallucinations, delusions and cognitive disorganization, affects roughly 1 percent of the U.S. population.* Many of those afflicted, however, also have reduced reproductive fitness, which means they are less likely to pass a genetic profile associated with the condition onto their offspring.

"It's sort of a genetic paradox," explains Steve Dorus, an evolutionary geneticist at the University of Bath in England. "Why is this disease found at such a high prevalence?"

Dorus co-authored a report, appearing in this week's *Proceedings of the Royal Society B*, about the evolution of genes linked to schizophrenia. After analyzing human DNA from several populations around the world and examining primate genomes dating back to the shared ancestor of both humans and chimpanzees, researchers reached a striking conclusion that several gene variants linked to schizophrenia were actually *positively* selected and remained largely unchanged over time, suggesting that there was some advantage to having them.

"Schizophrenia can be explained by a lot of individual alleles (variations of genes)," Dorus notes. "There are many different loci that impact the actual manifestation of the disease." Over the past decade, several dozen genes have been identified as potential culprits, and scientists believe that several genes cause disruptions in protein formations predisposing a person to schizophrenia.

For this study, the team, which also included Bernard Crespi, an evolutionary biology professor at Simon Fraser University in British Columbia, and East Carolina University evolution professor Kyle Summers, focused on 76 gene variations most strongly related to schizophrenia. By comparing these combinations with the evolution of other genes known to affect neuronal processes, the researchers determined that 28 of the schizophrenia-associated genes have been evolutionarily preferred in recent years by either Caucasian, Asian or African populations.

"Because it's a such a complex genetic trait ... you actually expect there to be some variability from population to population, in terms of what genes are playing a role in the disorder," Dorus says. He notes that he was surprised that the study turned up a positive selection for some of the genes most closely associated to the disease, including *DISC1* (*disrupted in schizophrenia 1*), which is involved in the transport of proteins along the relatively lengthy cell bodies of neurons, among them. "The most important thing is we don't really know what the basis of the selection has been," he says. "It could be due to an entire range of neurodevelopmental processes."

Co-author Crespi says that a number of theories have been floating around regarding the persistence of schizophrenia's genetic underpinnings. One holds that schizophrenia is a "disorder of language" and that the illness is an unfortunate consequence of the development of human speech, expression and creativity. "Whenever you get strong selection, it's like a big plus, and you can drag along a lot of minuses," he says. "You can think of schizophrenics as paying the price of all the cognitive and language skills that humans have—they have too many of the alleles that taken individually...might have positive effect, but together they are bad."

Dorus says the team will now home in on the 28 genes fingered in positive selection in the hope of finding new treatments for the mysterious disorder.

CORRECTION: *Initially, this phrase read "Schizophrenia, the psychotic disorder marked by hallucinations, multiple personalities and cognitive disorganization, affects roughly 1 percent of the U.S. population." The condition of having multiple personalities was incorrectly identified as a signature of schizophrenia.*

ABOUT THE AUTHOR(S)

Nikhil Swaminathan

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