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Schizophrenia candidate genes affect even healthy individuals

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Do gene variants that convey risk for schizophrenia affect apparently healthy individuals? Although these genes are present in every human, individuals may have different versions of these genes, called alleles. While many people who possess these “risk alleles” do not end up with schizophrenia, this does not mean they are unaffected by the presence of the risk allele.

In the largest study of its kind to date, scheduled for publication in the October 1st issue of *Biological Psychiatry*, researchers sought to examine the impact of a few particular genes, known to be associated with a diagnosis of schizophrenia, on a healthy population.

Stefanis and colleagues recruited more than 2000 young men and measured dimensions of their cognitive abilities that tend to be impaired in individuals diagnosed with schizophrenia. The authors also measured schizotypal personality traits, which represent behaviors that are associated with schizophrenia, such as atypical behaviors and beliefs, suspiciousness or paranoia, and discomfort in social situations.

They then genotyped these volunteers in relation to the four most prominent schizophrenia candidate genes: Neuregulin1 (NRG1), Dysbindin (DTNBP1), D-amino-acid oxidase activator (DAOA), and D-amino-acid oxidase (DAAO).

According to Nicholas Stefanis, the lead author on the paper, their study showed “that apparently normal individuals who posses several risk

alleles within these susceptibility schizophrenia genes, have indeed minute decrements in cognitive ability such as decreased attentional capacity and worse performance on memory tasks, and alterations in schizotypal beliefs and experiences." In other words, they found that the healthy individuals who possessed the risk variants within the DNTBP1, NRG1, and DAAO genes exhibited small reductions in their cognitive performance and had atypical experiences that might be associated with schizophrenia.

John H. Krystal, M.D., Editor of Biological Psychiatry and affiliated with both Yale University School of Medicine and the VA Connecticut Healthcare System, notes: "The genetics of schizophrenia is turning out to be a complicated story involving many so-called "risk gene variants" that are actually commonly present in the general population, i.e., people who do not have schizophrenia and will never develop this disorder.

It is striking that these genes all effect the glutamate system in the brain. Glutamate is the main excitatory chemical messenger used by the cerebral cortex. Thus, this paper highlights a role for glutamate in the development of schizophrenia-like symptoms, attention deficits, and memory problems. This genetic information adds to a growing body of evidence that highlights the potential importance of glutamate systems as a target for new medications for the treatment of schizophrenia."

Dr. Stefanis, explaining the importance of this study, comments that "these findings support the notion that even at the general population level, the genetic liability to psychosis may be expressed as minute and 'undetected to the naked eye' alterations in brain information processing capacity and behavior." Dr. Krystal adds, "Consistent with a growing body of evidence, this study suggests that there may be subtle cognitive impairments that are present when these common risk gene variants are present in the general population." Clearly, these findings will have an important impact on the future genetic work in this area.

Source: Elsevier