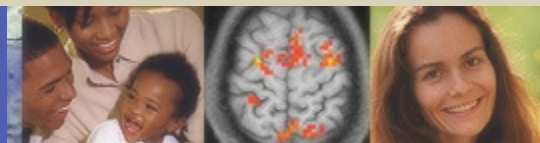




National Institute of Mental Health

Reducing the burden of mental illness and behavioral disorders through research on mind, brain, and behavior

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January 2, 2008

Ethnicity Predicts How Gene Variations Affect Response to Schizophrenia Medications

Different variations in the same gene influence how well different ethnic groups, and people within the same ethnic group, respond to various antipsychotic medications, report NIMH-funded researchers. If confirmed, their findings could one day help clinicians predict which medication is most likely to help a patient, based on his or her genetic makeup.

A medication that works well for one person with schizophrenia often doesn't work well for another. Genetic variations are thought to play a key role in this difference in response. While patients search for the right medications, their illnesses may worsen. Studies such as this one are aimed at discovering how specific gene variations affect patients' responses to specific medications, to better match patients to treatments.

The gene containing the variations, RGS4, had been implicated in schizophrenia in previous studies. It makes a protein that is thought to regulate the effects of receptors found on brain cells. The receptors, called G-protein coupled receptors, are known to be targets of antipsychotic medications.

Results of the study were reported in the January 1 issue of *Biological Psychiatry*, by Daniel Campbell, Ph.D., Pat Levitt, Ph.D., Patrick Sullivan, M.D., and colleagues from Vanderbilt University, University of North Carolina at Chapel Hill, Columbia University, and Karolinska Institute.

In this study, researchers compared how people of different ancestry responded to five different medications, then looked at which variations they had in their RGS4 genes. The 678 patients had taken part in the NIMH-funded Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). They included 198 people of African descent, 397 people of European descent, and 83 people of other ancestries.

Highlights of the findings are shown below.

Focusing on variations in the gene RGS4, researchers found that:

- Perphenazine and the newer medication olanzapine were particularly effective in African-descent patients with certain variations in the gene.
- Patients of African ancestry with a certain variation responded better to the medication perphenazine than to the newer medications quetiapine and ziprasidone.
- Variations in the gene predicted how well patients of European ancestry responded to the newer medication risperidone.

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▪ Differences in response to ziprasidone were striking. During treatment with ziprasidone, schizophrenia symptoms actually worsened in patients of African descent with certain variations of the gene. However, in those with a different variation, ziprasidone was as effective as other treatments. The same genetic variations did not have the same predictive value for ziprasidone in European-ancestry patients.

Reference

Campbell DB, Ebert PJ, Skelly T, Stroup TS, Lieberman J, Levitt P, Sullivan PF. Ethnic Stratification of the Association of RGS4 Variants with Antipsychotic Treatment Response in Schizophrenia. *Biological Psychiatry*. 2008 Jan 1;63(1):32-41. Epub 2007 Jun 22. PMID: 17588543

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