Spontaneous mutations widespread in non-familial schizophrenia

People with schizophrenia from families with no history of the illness were found to harbor eight times more spontaneous mutations - most in pathways affecting brain development - than healthy controls, in a study supported in part the National Institutes of Health's (NIH) National Institute of Mental Health (NIMH). By contrast, no spontaneous mutations were found in people with schizophrenia who had family histories of the illness.

“Our findings strongly suggest that rare, spontaneous mutations likely contribute to vulnerability in cases of schizophrenia from previously unaffected families,” said Maria Karayiorgou, M.D., of Columbia University, who led the research team. “This may also shed light on why the illness has frustrated efforts to implicate gene variants with major effects, and seems to defy natural selection by persisting in the population even though relatively few of those affected have children.”

Karayiorgou and her colleagues report on their whole genome study online in *Nature Genetics*, May 30, 2008.

"Such abnormal deletions or duplications of genetic material are increasingly being implicated in schizophrenia and autism ([http://www.nimh.nih.gov/science-news/2008/autism-gene-scans-converge-on-two-suspect-sites-two-types-of-genetic-risk.shtml](http://www.nimh.nih.gov/science-news/2008/autism-gene-scans-converge-on-two-suspect-sites-two-types-of-genetic-risk.shtml))," explained NIMH Director Thomas R. Insel, M.D. "Now we have a dramatic demonstration that genetic vulnerabilities for these illnesses may not be inherited from parents, at least in the sense that these vulnerabilities were not present in the parental genome. This line of research holds promise for improved treatments - and perhaps someday even prevention - of developmental brain disorders."

Although it's known that genetics plays a major role in the transmission of both autism and schizophrenia, most cases are sporadic rather than familial.

Echoing findings of another recent study ([http://www.nimh.nih.gov/science-news/2008/rates-of-rare-mutations-soar-three-to-four-times-higher-in-schizophrenia.shtml](http://www.nimh.nih.gov/science-news/2008/rates-of-rare-mutations-soar-three-to-four-times-higher-in-schizophrenia.shtml)), Karayiorgou and her colleagues determined that most of the suspect mutations were not random, but found in genes and pathways involved in brain development. However, whether a mutation was spontaneous or inherited was not determined for most of the subjects included in the earlier study.

To pinpoint the sources of the glitches, the researchers in the new study compared genetic data from 369 subjects with data from their biological parents - in a total sample of 1,077
individuals drawn from the European ancestry Afrikaner population in South Africa. Including parental genes makes it possible to definitively determine what's inherited.

Scans of each person's genome detected the spontaneous mutations in 15 of 152 individuals (10 percent) with non-familial schizophrenia, and only in two of 159 people (1 percent) without the illness - the eight-fold difference. Such sporadic cases were only 1.5 times more likely than controls to harbor inherited mutations.

The researchers also found three deletions of genetic material at a site on chromosome 22 previously implicated in schizophrenia, confirming it as the only known recurrent such mutation linked to schizophrenia. In addition to NIMH, the current study also cites support from the NIH's National Cancer Institute, National Institute of Diabetes and Digestive and Kidney Diseases, National Eye Institute, and the Lieber Center for Schizophrenia Research at Columbia University.

The National Institute of Mental Health (NIMH) mission is to reduce the burden of mental and behavioral disorders through research on mind, brain, and behavior. More information is available at the NIMH website, http://www.nimh.nih.gov.

The National Institutes of Health (NIH) - The Nation's Medical Research Agency - includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases.