



Schizophrenia is a chronic and disabling brain disorder that affects 2.4 million Americans, according to the 2005 National Comorbidity Survey-Replication. People with schizophrenia may hear voices other people don't hear or have a false belief that others are plotting to harm them. As with most illnesses, schizophrenia symptoms can range from mild to severe and can cause fearfulness, withdrawal, or extreme agitation. People with schizophrenia may not make sense when they talk, may not move or talk much, or can seem perfectly fine until they say what they are really thinking. It's often hard for people with schizophrenia to hold a job or take care of themselves, so the impact on their families and society is significant.

Yesterday

- Doctors, patients, and families viewed schizophrenia, one of the most devastating mental illnesses, as the result of bad parenting rather than as a developmental brain disease.
- There were no consistent guidelines for the diagnosis of this disorder.
- The medical treatments used to reduce hallucinations and delusions were complicated by neurologic side effects, including a severe movement disorder.
- In 1971, an estimated 433,000 people with mental disorders were institutionalized.

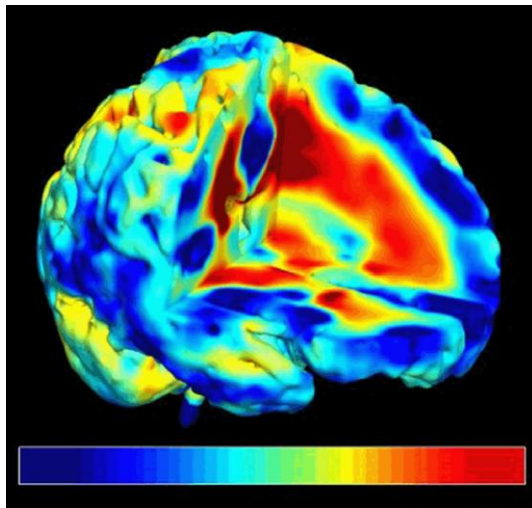
Today

- Schizophrenia is understood as a developmental brain disorder, involving specific pathways related to the prefrontal cortex.
- There are now reliable tools for diagnosing schizophrenia, as well as effective medical therapies that can reduce hallucinations and delusions with few neurologic side effects.
- Using advanced tools and methods for studying disease genetics, researchers have identified a number of possible susceptibility genes and are closer than ever to understanding how these genes may affect brain development and function in schizophrenia. Findings from such studies include:

- A shortened version of the “disrupted in schizophrenia” (DISC1) gene is over-expressed during fetal brain development in people with schizophrenia. DISC1 normally produces a protein involved in mood and memory, both of which are disturbed in schizophrenia. Since different genetic variations in DISC1 can lead to overproduction of the same shortened DISC1 gene product, this study helps to connect past, seemingly unrelated, findings.
- Deleting a specific type of glutamate receptor—glutamate being a brain chemical involved in communication between brain cells—early in life produces schizophrenia-like symptoms in mice. More notably, the mice developed these symptoms over time, resembling how the disorder develops in humans. In addition to supporting this mouse model for further research on schizophrenia, the finding provides strong support for causative theories involving this specific glutamate receptor.
- Studies examining whole genomes—the entire genetic code of a living thing—suggest that schizophrenia is genetically related to bipolar disorder, another serious mental illness characterized by severe fluctuations in mood, energy, and ability to function. The finding suggests that different mental disorders may arise from common vulnerabilities in brain development.

- Research on the “prodromal” stage of schizophrenia, which precedes a person’s first psychotic episode, has identified factors that may predict schizophrenia in up to 80 percent of youth who are at high risk of developing the illness.
- Though most cases start during a person’s late teens to early 20s or 30s, awareness of childhood-onset schizophrenia is increasing. Imaging studies have shown that growth of the brain’s long distance connections, called white matter, is stunted and lopsided in children who develop psychosis before puberty, with slower growth associated with worse outcomes. NIH researchers

suggest this phenomenon may represent a “window of opportunity” for future treatment interventions.



MRI scan data for childhood-onset schizophrenia. Areas colored in light and dark blue show fastest tissue loss, while yellow, orange, and red areas show fastest brain growth. Source: NIMH Child Psychiatry Branch

- For the first time, strategies to personalize treatment are available based on a large, NIH-funded, comprehensive study of available medications.
- In terms of quality of care, identifying treatments that don't work is as important as finding those that do. An NIH-funded study on early onset schizophrenia found that most children and teens stop treatment with antipsychotic medications due to serious side effects that included weight gain, anxiety, and metabolic changes linked to heart disease and diabetes. Such research emphasizes the need for safe and effective ways to treat chronic mental illness among youth populations.
- Even with the best treatments available, most patients with schizophrenia do not recover fully; they have basic problems in the way their brains manage attention and planning, which none of today's treatments target. Over the past three years, NIH has prioritized partnerships with private industry to develop effective treatments that target these cognitive deficits.

Tomorrow

- Finding ways to control metabolic side effects of atypical antipsychotic medications in youth is the goal of a

currently ongoing, NIH-funded study. The results will help determine better long-term treatment options for children and adolescents with schizophrenia or other major mental disorders (<http://www.nimh.nih.gov/science-news/2008/new-study-to-evaluate-ways-to-control-metabolic-side-effects-of-antipsychotics.shtml>).

- An NIH network focusing on prevention research—including diagnosis of schizophrenia before the first psychotic episode—may help reduce the burden of severe mental illnesses, which currently is largely attributable to underdiagnosis and undertreatment.
- In conjunction with prevention efforts, NIH is also supporting a large-scale research project to explore whether using early and aggressive treatment, individually targeted and integrating a variety of different therapeutic approaches, *after* the first psychotic episode will reduce symptoms and prevent the gradual deterioration of functioning that is characteristic of chronic schizophrenia (<http://www.nimh.nih.gov/health/topics/schizophrenia/raise/index.shtml>).
- People with mental illnesses smoke or use tobacco at higher rates than those without mental illnesses. Though generally believed to be a method of self-medication, little research has been done to confirm this link. According to an expert panel convened by NIH, research on smoking in this population can provide insights into the mechanisms that contribute to both tobacco dependence and psychiatric disorders. In addition, research into adapting smoking cessation programs for psychiatric populations is needed (<http://www.nimh.nih.gov/science-news/2009/expert-panel-addresses-high-rates-of-smoking-in-people-with-psychiatric-disorders.shtml>).
- A large-scale study on “epigenetics” in schizophrenia—environmentally triggered changes in gene expression—seeks to reveal how factors like diet, chemicals, infections, and life experience impact genetic risk. Because some epigenetic changes may be reversible, this research may lead to new ways to treat schizophrenia (<http://www.nimh.nih.gov/science-news/2008/study-probes-environment-triggered-genetic-changes-in-schizophrenia.shtml>).

For more information, please contact the NIMH Information Center at nimhinfo@nih.gov or 301-443-4513.

National Institute of Mental Health (NIMH):

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