

## Scientists demonstrate link between genetic defect and brain changes in schizophrenia

October 16 2009

---

For decades, scientists have thought the faulty neural wiring that predisposes individuals to behavioral disorders like autism and psychiatric diseases like schizophrenia must occur during development. Even so, no one has ever shown that a risk gene for the disease actually disrupts brain development.

Now, researchers at the University of North Carolina at Chapel Hill School of Medicine have found that the 22q11 gene deletion - a mutation that confers the highest known genetic risk for [schizophrenia](#) - is associated with changes in the development of the [brain](#) that ultimately affect how its circuit elements are assembled.

In studies conducted in mice, the researchers discovered that the genetic lesion alters the number of a critical subset of neurons that end up in the brain's [cerebral cortex](#) - the region critical to reasoning and memory. The defect also causes another type of nerve cell - called GABAergic neurons - to be misplaced within the brain's cortical layers, resulting in a subtle miswiring of the organ.

"For practically every other disease, we know what cells take a hit," said senior study author Anthony LaMantia, Ph.D., professor of cell and molecular physiology and co-director of the Silvio M. Conte Center for Research in Mental Disorders at the UNC School of Medicine. "For multiple sclerosis the myelinating oligodendrocytes in the brain falter, for Lou Gehrig's disease the [motor neurons](#) in the brain stem degenerate. But we really had no idea what was happening in schizophrenia, or in

any of the psychiatric diseases for that matter - until now."

His study will be presented Oct. 17 at the Society for Neuroscience meeting in Chicago, by Daniel Meechan, Ph.D., post-doctoral fellow in the LaMantia laboratory and the first author of a recent paper in [Proceedings of the National Academy of Sciences](#) that details the findings.

The study lends the first clear support to the "neurodevelopmental hypothesis" - a scientific theory LaMantia calls the "Hail Mary" of schizophrenia pathologists.

For many years, researchers searched in vain for any indication that the brains of patients with schizophrenia were different from normal subjects --for some laboratory finding along the lines of the plaques and tangles characteristic of Alzheimer's disease or the degeneration of dopamine cells that are the calling card of Parkinson's disease. Similar degenerative change has never been identified for schizophrenia. Finally they proposed that the defects in schizophrenia must arise before the brain is fully formed, rather than after.

Then researchers began to discover regions of the genome -- many of which had neurodevelopmental functions -- that made people susceptible to schizophrenia.

In this study, LaMantia and his colleagues decided to pursue deletion of one such region on human chromosome 22, which causes DiGeorge syndrome in humans, because it is the single best-defined genetic lesion associated with schizophrenia. They tracked two subclasses of neural stem cells -- called basal and apical progenitors -- throughout early [brain development](#) in a mutant mouse with the same genetic deletion. They found that the basal progenitors divided more slowly than they should, and as a result the cells that they give rise to in the cortex were not

generated in the proper numbers.

The researchers also looked at another population of cells, the GABAergic cells that are thought to essentially put the brakes on electrical activity in mature cortical circuits. The function of these cells is believed to be one of last processes to be disrupted in the schizophrenic brain. LaMantia found that these GABAergic neurons never made their way to their correct positions in the cortical layers of the brain of the mouse model of DiGeorge Syndrome .

The researchers would now like to figure out how these alterations in the circuitry of the brain affect the behavior of the mouse. They also hope that understanding the "mis-wiring" of the brain in a genetic animal model of schizophrenia would help them understand the causes of the disease in the general population.

"Now that we know what cells can be affected in schizophrenia, it opens up new avenues in thinking about the molecular mechanisms underlying this and other psychiatric illnesses," said LaMantia. "We can even begin to look for biomarkers of the disease that can be used for better diagnosis and treatment."

Source: University of North Carolina School of Medicine ([news](#) : [web](#))

Citation: Scientists demonstrate link between genetic defect and brain changes in schizophrenia (2009, October 16) retrieved 19 April 2024 from <https://medicalxpress.com/news/2009-10-scientists-link-genetic-defect-brain.html>

|  |
|--|
| <p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p> |
|--|