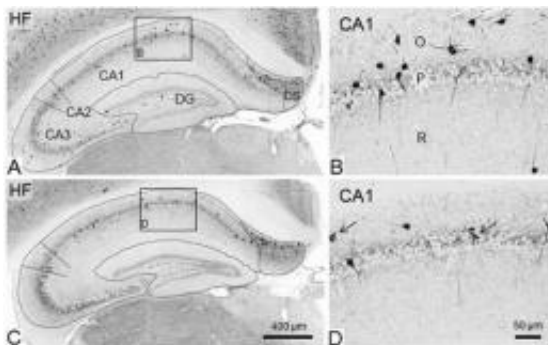


Study links schizophrenia genetics to disruption in how brain processes sound

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Staining performed by Konrad Talbot, PhD, targeting a marker for nerve cells involved in inhibition are shown in cross sections of the hippocampus, which is a part of the brain known to be affected in schizophrenia and involved in memory and cognition. In normal mice (top; A and B) a number of inhibitory cells are found. This staining is reduced in mice with reduced dysbindin (bottom; C and D). The finding is identical to that found in tissue from schizophrenia patients and supports the functional finding of the paper that fast inhibitory processes are disrupted in schizophrenia, leading to symptoms of the disease. Credit: Konrad Talbot, PhD, Perelman School of Medicine, University of Pennsylvania, Neuron

(Medical Xpress) -- Recent studies have identified many genes that may put people with schizophrenia at risk for the disease. But, what links genetic differences to changes in altered brain activity in schizophrenia is not clear. Now, three labs at the Perelman School of Medicine at the University of Pennsylvania have come together using electrophysiological, anatomical, and immunohistochemical approaches

- along with a unique high-speed imaging technique - to understand how schizophrenia works at the cellular level, especially in identifying how changes in the interaction between different types of nerve cells leads to symptoms of the disease. The findings are reported this week in the [Proceedings of the National Academy of Sciences](#).

"Our work provides a model linking genetic risk factors for [schizophrenia](#) to a functional disruption in how the brain responds to sound, by identifying reduced activity in special nerve cells that are designed to make other cells in the brain work together at a very fast pace" explains lead author Gregory Carlson, PhD, assistant professor of Neuroscience in Psychiatry. "We know that in schizophrenia this ability is reduced, and now, knowing more about why this happens may help explain how loss of a protein called dysbindin leads to some symptoms of schizophrenia."

Previous genetic studies had found that some forms of the gene for dysbindin were found in people with schizophrenia. Most importantly, a prior finding at Penn showed that the dysbindin protein is reduced in a majority of schizophrenia patients, suggesting it is involved in a common cause of the disease.

For the current PNAS study, Carlson, Steven J. Siegel, MD, PhD, associate professor of Psychiatry, director of the Translational Neuroscience Program; and Steven E. Arnold, MD, director of the Penn Memory Center, used a mouse with a mutated dysbindin gene to understand how reduced dysbindin protein may cause symptoms of schizophrenia.

The team demonstrated a number of sound-processing deficits in the brains of mice with the mutated gene. They discovered how a specific set of nerve cells that control fast brain activity lose their effectiveness when dysbindin protein levels are reduced. These specific [nerve cells](#)

inhibit activity, but do so in an extremely fast pace, essentially turning large numbers of cells on and off very quickly in a way that is necessary to normally process the large amount of information travelling into and around the brain.

Other previous work at Penn in the lab of Michael Kahana, PhD has shown that in humans the fast brain activity that is disrupted in mice with the dysbindin mutation is also important for short-term memory. This type of [brain activity](#) is reduced in people with schizophrenia and resistant to current therapy. Taken as a whole, this work may suggest new avenues of treatment for currently untreatable symptoms of schizophrenia, says Carlson.

Additional co-authors are: Konrad Talbot, Tobias B. Halene, Michael J. Gandal, Hala A. Kazi, Laura Schlosser, Quan H. Phung, and Raquel E. Gur, all from the Department of Psychiatry at Penn.

Provided by University of Pennsylvania School of Medicine

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