# Gene malfunctions cause schizophrenia, depression symptoms

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Researchers have demonstrated for the first time that malfunction of a gene that had been associated with schizophrenia and depression does indeed cause symptoms of those disorders. They said their findings in mice offer a possible animal model for developing treatments for schizophrenia and depression. Also, they said their findings support the theory that the two disorders share common genetic mechanisms.

Steven Clapcote, David Porteous, John Roder, and colleagues reported their findings in the May 3, 2007 issue of the journal *Neuron*, published by Cell Press.

In their experiments, the researchers sought to explore the consequences of mutating a gene called "Disrupted in schizophrenia 1" (DISC1), which had been found in one family to be associated with schizophrenia, bipolar disorder, and major depression.

The researchers' theory was that different mutant variations of DISC1 might have different pathological effects. To test this theory, the researchers screened a large population of mouse mutants to isolate two with different mutations in DISC1.

They found that, indeed, one of the mutant mouse strains exhibited behavioral abnormalities and memory deficiencies resembling the symptoms of schizophrenia in humans. Additionally, these symptoms could be alleviated in the mice by antipsychotic drugs.

Similarly, the other mutant mouse strain showed behaviors that reflected depressive symptoms. These symptoms could be alleviated by an antidepressant, found the researchers.

Both types of DISC1 mutant mice exhibited the same kind of reduced brain volume seen in people with schizophrenia and depression, the researchers found. Also, both types showed biochemical abnormalities in the function of the protein produced by the DISC1 gene.

The researchers concluded that the different effects of antipsychotic and antidepressant drugs on the two mutant strains "might provide clues to effective medications for these patient groups. Indeed, these mice could represent a model system to explore novel treatment and preventative strategies for certain symptoms of major mental illness," they wrote.

"We have shown that two independent missense mutations in mouse Disc1 elicit distinct physiological, pharmacological, neuroanatomical, and behavioral phenotypes, which when taken together are strikingly consistent with the emerging picture from clinical and basic studies of DISC1 as a common genetic and biologically plausible risk factor for major mental illness," concluded Clapcote and colleagues. They wrote that "our findings lend further credence to the growing recognition that schizophrenia and bipolar disorder share, at least in part, common genetic etiologies and thus underlying molecular mechanisms."

Source: Cell Press