Hopkins team develops first mouse model of schizophrenia

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Johns Hopkins researchers have genetically engineered the first mouse that models both the anatomical and behavioral defects of schizophrenia, a complex and debilitating brain disorder that affects over 2 million Americans.

In contrast to current animal studies that rely on drugs that can only mimic the manifestations of schizophrenia, such as delusions, mood changes and paranoia, this new mouse is based on a genetic change relevant to the disease. Thus, this mouse should greatly help with understanding disease progression and developing new therapies.

Animal models of schizophrenia have been hard to design since many different causes underlie this disease. However, Akira Sawa, M.D., Ph.D., associate professor of psychiatry and neuroscience and director of the program in molecular psychiatry and his colleagues took advantage of the recent discovery of a major risk factor for this disease: the DISC1 gene (short for disrupted in schizophrenia), which makes a protein that helps nerve cells assume their proper positions in the brain.

As reported online this week in *Proceedings of the National Academy of Sciences*, the researchers generated mice that make an incomplete, shortened form of the DISC1 protein in addition to the regular type. The short form of the protein attaches to the full-length one, disrupting its normal duties.

As these mice matured, they became more agitated when placed in an

open field, had trouble finding hidden food, and did not swim as long as regular mice; such behaviors parallel the hyperactivity, smell defects and apathy observed in schizophrenia patients. Magnetic resonance imaging (MRI), taken in collaboration with Susumu Mori, Ph.D., professor of radiology, also revealed characteristic defects in brain structure, including enlarged lateral ventricles, a region that circulates the spinal fluid and helps protect against physical trauma.

Sawa notes that the defects in these mice were not as severe as those typically seen in people with schizophrenia, because more than one gene is required to trigger the clinical disease. “However, this mouse model will help us fill many gaps in schizophrenia research,” he says. “We can use them to explore how external factors like stress or viruses may worsen symptoms. The animals can also be bred with other strains of genetically engineered mice to try to pinpoint additional schizophrenia genes.”

Source: Johns Hopkins Medical Institutions