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Researchers discover new link to schizophrenia

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Neuroscientists at Johns Hopkins have discovered that mice lacking an enzyme that contributes to Alzheimer disease exhibit a number of schizophrenia-like behaviors. The finding raises the possibility that this enzyme may participate in the development of schizophrenia and related psychiatric disorders and therefore may provide a new target for developing therapies.

The BACE1 enzyme, for beta-site amyloid precursor protein cleaving enzyme, generates the amyloid proteins that lead to Alzheimer's disease. The research team years ago suspected that removing BACE1 might prevent Alzheimer.

"We knew at the time that in addition to amyloid precursor protein, BACE1 interacts with other proteins but we didn't know how those interactions might affect behavior," says Alena Savonenko, M.D., Ph.D., an assistant professor in neuropathology at Hopkins.

Reporting in the *Proceedings of the National Academies of Sciences*, the research team describes how mice lacking the BACE1 enzyme show deficits in social recognition among other behaviors classically linked to schizophrenia.

A normal mouse, when introduced to another mouse, shows a lot of interest the first time they meet. If the mice are separated then reintroduced, their interest drops because they remember having met before, a phenomenon the researchers call habituation. If they then

introduce a completely different mouse, interest piques again at the newbie.

The researchers introduced mice lacking BACE1 to another mouse. The first time they met, the BACE1 mouse showed interest, the second time meeting the same mouse the BACE1 mouse showed less interest and even less interest the third time. The researchers then introduced the BACE1 mouse to a totally different mouse of a different strain and the BACE1 mouse showed no interest at all. “These mice were totally disinterested, normal mice just don’t behave like this,” says Savonenko.

Additionally, the researchers found that these BACE1-lacking mice also displayed many other schizophrenia-like traits. Most importantly, according to Savonenko, some of the deficits improved after treatment with the antipsychotic drug clozapine.

Because schizophrenia is a disorder likely caused by many different factors, Savonenko explains that BACE1 might contribute to an increased risk of schizophrenia in certain patients and the BACE1 mice will be a useful animal model. “We never thought we would see one mouse that closely mimics so many of the clinical features of schizophrenia,” says Alena Savonenko, M.D., Ph.D., an assistant professor of neuropathology at Hopkins. “This could be a really useful model to study and understand the molecular contributions to the disease.”

Source: Johns Hopkins Medical Institutions