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Memory study on mice offers new insights into understanding autism

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Researchers at New York University's Center for Neural Science and the Baylor College of Medicine have identified a protein that when removed from mice results in behaviors that are akin to those with autism and obsessive-compulsive disorders. Their findings, which appear in the latest issue of the journal *Neuron*, may enhance our understanding of these and other neurological disorders.

The protein FKBP12, found in both humans and mice, is known to regulate mTOR, an enzyme involved in synaptic plasticity, or the ability of the neurons to change the collective strength of their connections with other neurons. Learning and memory are believed to result from changes in synaptic strength. mTOR also plays a role in behavioral plasticity—the ability to alter behavior in response to environmental changes.

The researchers eliminated FKBP12 from the brains of mice late in development and subsequently examined them for alterations in synaptic plasticity—specifically, in a brain area required for memory—and their behaviors. To test how different types of memory were affected by the absence of FKBP12, the NYU and Baylor scientists ran the mice through a variety of mazes and observed how they responded to certain objects.

The absence of the protein produced striking neurological and behavioral changes in the studied mice. Their results showed increased mTOR signaling, which regulates protein translation. This indicates that FKBP12 acts to limit mTOR activity. The researchers also found that the mice had enhanced synaptic plasticity and contextual memory,

suggesting that FKBP12 negatively regulates these processes.

However, based on additional behavioral studies, the researchers concluded that the brain's inability to properly regulate the activity of mTOR may have dire consequences. These findings showed that the mice had enhanced perseveration—that is, once they learned a task, such as how to navigate a maze, they had difficulty learning how to navigate a different version of the maze. They also displayed enhanced repetitive behaviors and were more likely to interact with familiar objects than they were with novel objects. These are behaviors often found in individuals suffering from autism and other neurological disorders.

"Our results suggest that FKBP12 regulates neuron signaling that curbs the manifestation of traits observed in several neurological disorders including autism, obsessive-compulsive disorder, and schizophrenia," said Eric Klann, an NYU neuroscientist and the lead researcher of the study. "Perseverative and repetitive behaviors associated with these neurological disorders are widely believed to be developmentally established—determined in utero by genetic, hormonal, and environmental factors. Because our study indicates that postnatal release of mTOR activity can result in certain perseverative behaviors, it challenges the idea that some aspects of these conditions are developmentally predetermined."

Source: New York University