Researchers identify a protein critical for memory, learning

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Researchers from the University of Toronto and The Hospital for Sick Children (Sick Kids) have made a breakthrough discovery that may eventually change the way physicians approach treatment of learning and memory defects in children and adults. Their findings are published in the current issue of *PLoS Biology*.

A team led by Dr. Roderick McInnes, a professor of pediatrics and molecular genetics, Anne and Max Tanenbaum Chair in Molecular Medicine at the University of Toronto and Sick Kids senior scientist, and Dr. Michael Salter, professor of physiology, Sick Kids senior scientist and head of the program in neurosciences and mental health, found that a protein called Neto1 is critical for memory and learning in mice.

The researchers discovered that Neto1 is a key component of synapses, the highly specialized sites of communication between the brain's individual neurons (nervous system cells). Mice genetically engineered to be deficient in Neto1 show a dramatic decrease in learning and in the way synapses adapt to brain activity.

"We have a new player in the game. Neto1 was never considered to be involved in how nerve cells communicate with one another. Now we found out that not only is it involved ... it's critical," said Salter.

To determine whether the learning defect in the mice could be improved, the scientists gave the Neto1-lacking mice a drug that is currently being clinically tested in patients with Alzheimer's disease.

Remarkably, in the mice with the inherited learning defect, learning and memory were restored to normal by the drug.

"It's part of a paradigm shift in neuroscience," said McInnes. "Neurologists and neuroscientists have always tended to think that if the brain is abnormal at birth, nothing can be done to improve intellectual function and that special education was virtually the only assistance available. "

"Our findings, and other research over the past five years suggest that the situation is more hopeful. It is no longer a fantasy to think that drug treatment might, in the future, be available for such patients."

Sick Kids post-doctoral fellows and the study's lead authors, David Ng and Graham Pitcher, said "The idea of using this type of drug, which belongs to class of drugs called ampakines, was that of our collaborator Dr. John Roder of the Samuel Lunenfeld Research Institute in Toronto. It was an inspired suggestion."

As promising as these findings are, it is still very early days before patients with intellectual disabilities could ever be offered a medication of this type. "We would be concerned about possible negative effects, including disordered thinking or emotional disturbances, which can't be fully evaluated in an animal model," said McInnes.

Provided by University of Toronto