Scientist discovers why drug boosts memory in Down syndrome mice

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(Medical Xpress) -- A University of Colorado School of Medicine researcher who found a drug that improved memory in mice with Down syndrome has unlocked the mystery of how it works.

In a new study published in Learning & Memory, Alberto Costa, MD, Ph.D., Associate Professor of Medicine and Neuroscience, and Graduate Assistant Jonah Scott-McKean found the mechanism behind excessive levels of long-term synaptic depression, or LTD, in mice with Down syndrome. LTD makes transmission of messages along the brain's synapses more difficult and is frequently referred to as a mechanism for forgetting.

The study proposes that the excess LTD is likely caused by the overrepresentation of a limited subset of genes contained in the extra chromosome carried by these mouse models of Down syndrome. The investigators also found that when the drug memantine was administered to these mice at doses similar to those used to treat Alzheimer's disease, LTD levels fell significantly. Therefore, Costa and Scott-McKean hypothesize that similar phenomena might also occur in the brains of persons with Down syndrome.

"We found the mechanism by which LTD is exaggerated in a mouse model of Down syndrome," Costa said. "We wanted to see if memantine would normalize the brain function of these mice. We found that the drug brings this important physiological parameter associated to learning and memory ice to near normal levels."

Costa found that this exaggerated LTD in Down syndrome mice does not share the same cellular mechanism as a similar phenomenon seen in a mouse that mimics the human disorder known as fragile X syndrome, which is the second most common form of intellectual disability of genetic origin. Costa had earlier discovered that memantine, currently used to treat patients with Alzheimer's disease, improved memory in mice with Down syndrome but exactly how was unclear. He recently completed the data collection phase of a clinical trial using the drug on about 40 people with Down syndrome. The results have not yet been published.

"This will help us develop rational therapies for different intellectual disabilities. For example, based on these findings, it is probably unlikely that certain compounds that are currently being tested for the treatment of fragile X would work in persons with Down syndrome and, conversely, it is unlikely that a drug like memantine might be of any help in the improvement of cognition of young individuals with fragile X" he said. "It will also help us in the planning of clinical trials and represents another move toward more personalized therapies."

Provided by University of Colorado Denver