Memantine drug shown to improve memory in those with Down syndrome

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Researchers at the University of Colorado School of Medicine have found a drug that boosts memory function in those with Down syndrome, a major milestone in the treatment of this genetic disorder that could significantly improve quality of life.

"Before now there had never been any positive results in attempts to improve cognitive abilities in persons with Down syndrome through medication," said Alberto Costa, MD, Ph.D., who led the four- year study at the CU School of Medicine. "This is the first time we have been able to move the needle at all and that means improvement is possible."

The study was published today in the journal *Translational Psychiatry.*

Costa, an associate professor of medicine, and his colleagues studied 38 adolescents and young adults with Down syndrome. Half took the drug memantine, used to treat Alzheimer's disease, and the others took a placebo.

Costa's research team hypothesized that memantine, which improved memory in mice with Down syndrome, could increase test scores of young adults with the disorder in the area of spatial and episodic memory, functions associated with the hippocampus region of the brain.

Participants underwent a 16-week course of either memantine or a placebo while scientists compared the adaptive and cognitive function of the two groups.

While they found no major difference between the groups in adaptive and most measures of cognitive ability, researchers discovered that those taking memantine showed significant improvement in verbal episodic memory. One of the lowest functioning individuals in the study saw a ten-fold increase in memory skills.

"People who took the medicine and memorized long lists of words did significantly better than those who took the placebo," said Costa, a neuroscientist specializing in Down syndrome research. "This is a first step in a longer quest to see how we can improve the quality of life for those with Down syndrome."

Currently, there are drugs that treat the symptoms of medical conditions associated with Down syndrome but nothing to improve brain function.

But in 2007 Costa demonstrated that memantine could improve memory in mice with Down syndrome. He then set out to replicate those findings in a human trial of the drug.

"This is an excellent example of translational science," he said. "We took a drug that worked well in mice and we tested it in humans with positive results."

Although the trial was small, the results could have far-reaching implications. Costa said a follow-up study was needed using a larger group of people with Down syndrome. Another important step will be to pursue studies with younger, school-age participants with Down syndrome. They would have more rapidly developing brains and, since they are in school, would be routinely tested so the effects of the drug could be closely monitored. That could take as little as five years.

Researchers also want to know if memantine can ward off the onset of Alzheimer's disease in those with Down syndrome. The two conditions

show striking similarities and researchers are actively exploring how they may be linked. Babies born with Down syndrome, for example, often carry the biological markers for Alzheimer's disease.

"Everyone with Down syndrome will develop Alzheimer's disease pathology by their mid-30s," Costa said. "We would like to know if this drug can slow down or even halt the development of that disease in adults with Down syndrome."

Memantine works by normalizing the function of a glutamate receptor in the brain known as the N-methyl-D-aspartate or the NMDA receptor.

"This receptor plays a central role in memory and learning," Costa said.

Given the small size of the study and the need for more research, Costa stressed that people should not start taking memantine for Down syndrome. Although it has proven safe and well-tolerated by the study participants, researchers urge caution, saying more work needs to be done to determine if this is a viable treatment option.

"Our study is a significant and hopeful sign that certain drugs can enhance the intellectual capacity of those with Down syndrome," he said. "For more than 30 years we have been unable to impact cognition in Down syndrome. Now it appears that we may be able to."

Costa has a major stake in improving the lives of those with Down syndrome, the most common cause of intellectual disability. He has a 17-year-old daughter with the condition.

"For me this research is not merely academic," he said. "It's personal."

The CU School of Medicine's work on Down syndrome has resulted in it being chosen as one of nine national testing centers for a new drug

manufactured by F. Hoffmann-La Roche LTD aimed at improving memory in adults with Down syndrome. Costa is the principal investigator of the Colorado center.

He will give a lecture about his latest research July 20 in Washington D.C. at the 2012 Annual Meeting & Clinical Symposium of the Down Syndrome Medical Interest Group - USA. The conference is being held from 1 p.m. to 9 p.m. at the Marriott Wardman Park, 2660 Woodley Rd. NW.

The other researchers in the study included Richard Boada, Ph.D., Christa Hutaff-Lee, Ph.D., David Weitzenkamp, Ph.D., Timothy A. Benke, MD, Ph.D. and Edward J. Goldson, MD.

The trial was funded by Forest Research Institute Investigator Initiated Grant NAM-58. During the course of this study, Costa was also supported in part by grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

"I also am grateful to the Anna and John J. Sie Foundation, the Linda Crnic Institute and the Coleman Institute for Cognitive Disabilities for believing in my research all these years. This work would not have been possible without their support in these harsh economic times," Costa said.

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