

New targeted drug for treating fragile X syndrome, potentially autism, is effective

September 19 2012

An investigational compound that targets the core symptoms of fragile X syndrome is effective for addressing the social withdrawal and challenging behaviors characteristic of the condition, making it the first such discovery for fragile X syndrome and, potentially, the first for autism spectrum disorder, a study by researchers at the UC Davis MIND Institute and Rush University Medical Center, Chicago, has found.

The finding is the result of a clinical trial in adult and pediatric subjects with [fragile X syndrome](#). It suggests, however, that the compound may have treatment implications for at least a portion of the growing population of individuals with [autism spectrum disorder](#), as well as for those with other conditions defined by social deficits. The study is published online today in the journal *Science Translational Medicine*. A second study by the manufacturer of the compound is included in the same issue.

The "first-in-patient" drug trial was led by internationally recognized fragile X researchers Elizabeth Berry-Kravis of Rush University Medical Center and Randi Hagerman of the UC Davis [MIND Institute](#). It examined the effects of the compound STX 209, also known by the name arbaclofen.

The study was conducted collaboratively with Seaside Therapeutics, a Cambridge, Mass., pharmaceutical company that is focused on translating bench research on fragile X and autism into therapeutic interventions. Seaside Therapeutics produces the compound.

"This study shows that STX 209 is an important part of the treatment for fragile X syndrome, because it improved symptoms in those with significant [social deficits](#) or autism as well as fragile X syndrome," said Hagerman, medical director of the MIND Institute. "Additional studies also are suggesting that STX 209 can be helpful for autism without fragile X syndrome. Until now, there have been no targeted treatments available for autism. This appears to be the first."

Fragile X syndrome is the most common known cause of inherited intellectual impairment, formerly referred to as mental retardation, and the leading known single-gene cause of autism. Social impairment is one of the core deficits in both fragile X and autism. The U.S. Centers for Disease Control and Prevention (CDC) estimates that about 1 in 4,000 males and 1 in 6,000 to 8,000 females have the disorder. An estimated 1 in 88 children born today will be diagnosed with autism, according to the CDC.

"There are no Food and Drug Administration-approved treatments for fragile X syndrome, and the available options help secondary symptoms, but do not effectively address the core impairments in fragile X. This is the first large-scale study that is based on the molecular understanding of fragile X and suggests that the core symptoms may be amenable to pharmacologic treatment," said lead study author Elizabeth Berry-Kravis, professor of pediatrics, neurological sciences and biochemistry at Rush University Medical Center.

"This study will help to signal the beginning of a new era of targeted treatments for genetic disorders that have historically been regarded as beyond the reach of pharmacotherapy," Berry-Kravis said. "It will be a model for treatment of autism, intellectual disability and developmental brain disorders based on understanding of dysfunction in brain pathways, as opposed to empiric treatment of symptoms. We hope mechanistically based treatments like STX209 ultimately will be shown to improve

cognitive functioning in longer-term trials."

Studies in mice genetically engineered to exhibit features of fragile X, including social impairment, have suggested that the behavioral abnormalities in fragile X result from deficiencies in the neurotransmitter gamma-amino butyric acid (GABA). Decreased GABA has been observed in a mouse model of fragile X in many areas of the brain including the hippocampus, and has been hypothesized to be a basis of the social anxiety and avoidance characteristic of fragile X sufferers, the study says.

Arbaclofen is an agonist for gamma-amino butyric acid type B, or GABA-B, receptors. An agonist is a chemical that effectively combines with a receptor on a synapse to effect a physiologic reaction typical of a naturally occurring substance. Anxiety-driven repetitive behavior and social avoidance have been reduced in fragile X-engineered mice treated with arbaclofen. The current, first-of-its-kind study investigated whether arbaclofen would produce similar results in human subjects.

The double-blind, placebo-controlled clinical trial initially recruited 63 male and female subjects at 12 sites across the United States for the research, conducted between December 2008 and March 2010. The participants ranged in age from 6 to 39 years. Of the initial participants, 56 completed the clinical trial. There were no withdrawals related to drug tolerability. The majority of the subjects were treated with what was assessed as the optimum tolerated dosage of the study drug, 10 milligrams twice a day in younger patients and three times a day in adults. Compliance was monitored by patient guardians, who filled out a dosing form on a daily basis.

The study subjects returned for evaluations at two- and four-week intervals after beginning the six-week-long treatment. The drug then was tapered down over a one- to two-week period.

The effects of the medication were scored on variables of the Aberrant Behavior Checklist (ABC), a behavior-rating scale for the assessment of drug-treatment effects. The checklist includes variables for irritability, lethargy/withdrawal, stereotypic (repetitive) behavior and hyperactivity, among other factors.

The study found improvement for the full study population on the social-avoidance subscale, an analysis validated by secondary ratings from parent observation of improvement in subjects' three most problematic behaviors. It found that the medication was the same as placebo, however, on the subscale for irritability.

The study is one of several at the MIND Institute aiming to help improve behavior and cognition for individuals with fragile X syndrome and autism spectrum disorder.

Hagerman currently is leading a larger controlled trial of STX 209 at UC Davis that is also carried out at multiple centers and is enrolling individuals with fragile X syndrome from ages 5 to 50. Individuals interested in enrolling may contact Lindsey Partington at 916-703-0471 or via e-mail at lindsey.partington@ucdmc.ucdavis.edu.

"We are looking forward to further studies utilizing STX 209 in both [autism](#) and fragile X syndrome because the fragile X mouse studies demonstrate long-term strengthening of synaptic connections with continued use of this medication," Hagerman said.

Provided by UC Davis

Citation: New targeted drug for treating fragile X syndrome, potentially autism, is effective (2012, September 19) retrieved 3 May 2024 from <https://medicalxpress.com/news/2012-09-drug-fragile-syndrome-potentially-autism.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.