Promising new drug being evaluated as possible treatment option for fragile X syndrome

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A pilot trial of an oral drug therapy called fenobam has shown promising initial results and could be a potential new treatment option for adult patients with Fragile X syndrome (FXS). Findings of the open label, single-dose study by researchers at Rush University Medical Center and the University of California, Davis, Medical Center are to be published in the upcoming January issue of the *Journal of Medical Genetics*.

Results of an initial evaluation of the safety of fenobam, which is an mGluR5 antagonist, in adult males and females with Fragile X syndrome showed there were no adverse side effects from the medication.

"This is the first study assessing the safety and pharmokinetic metabolism of an mGluR5 antagonist in humans with Fragile X syndrome," said Dr. Elizabeth Berry-Kravis, pediatric neurologist at Rush and principal investigator of the study. "Also, some patients showed calmed behavior and rapid reduction in hyperactivity and anxiety, similar to effects of the drug in mouse models."

Fragile X syndrome is the most common inherited cause of mental impairment and the most common known cause of autism. Fragile X affects 1 in 4000 males and 1 in 6000 females of all races and ethnic groups (source Centers for Disease Control). About 1 in 259 women carry fragile X and could pass it to their children. About 1 in 800 men carry fragile X; their daughters will also be carriers. Symptoms of Fragile X syndrome include mental impairment such as learning disabilities, attention deficit, hyperactivity, autistic-like behaviors, and anxiety and unstable mood.

Fragile X syndrome is caused by lack of activity of the FMR1 gene, which is responsible for a protein called FMRP. Without FMRP, activation of cell pathways by a brain receptor protein called mGluR5 goes unchecked, and it has been theorized that this plays an important part in Fragile X syndrome.

To test this theory, past researchers have used laboratory mice without an active FMR1 gene, like in Fragile X syndrome, but with a reduced amount of mGluR5 protein. The mice showed an improvement in their brain structure and function, in their brains' ability to make key proteins, and in memory and body growth. This shows that the over-activation of mGluR5 is very important in Fragile X syndrome, and suggests a path for drug development to treat the syndrome.

In the current study, twelve participants recruited by Rush and the University of California, Davis received a single oral dose of 50-to-150 mg of fenobam. Prepulse inhibition (PPI) and continuous performance test (CPT) were obtained before and after dosing to explore the effects of fenobam on measures of sensory gating, attention and inhibition. In six of the 12 individuals there was a 20 percent improvement.

"Currently, there are no therapies on the market to treat cognitive deficits associated with Fragile X syndrome," said Berry-Kravis. "This pilot study has identified the potential beneficial clinical effects of fenobam, but further research is needed."

Source: Rush University Medical Center