

NEW DRUG SHOWS PROMISE FOR TREATMENT OF ADULTS WITH FRAGILE X SYNDROME

(SACRAMENTO, Calif.) A study by researchers at Rush University Medical Center, Chicago, and the UC Davis M.I.N.D. Institute has found that an oral drug therapy, called fenobam, shows promising results and could be an effective new treatment for adults with fragile X syndrome.

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

Berry-Kravis, a pediatric neurologist at Rush, said that some study subjects given fenobam showed calmed behavior and rapid reduction in hyperactivity and anxiety effects that are similar to the drug’s action in earlier studies involving mice.

The findings of the open-label, single-dose study were published online today in the *Journal of Medical Genetics*.

Fragile X syndrome is the most common inherited cause of intellectual disability, whose effects range from learning disabilities to more severe intellectual disabilities like mental retardation. Fragile X syndrome is also the most commonly known cause of autism or “autistic-like” behaviors. Fragile X syndrome affects one person in 3,000 worldwide.

“All children with autism or intellectual disability should be tested for the fragile X mutation,” said study senior investigator Randi Hagerman, a developmental and behavioral pediatrician and the UC Davis M.I.N.D. Institute’s medical director. “This targeted treatment for fragile X syndrome may be helpful for a subgroup of children with autism, too.”

The study is the first to assess the safety and pharmacokinetic metabolism of a type of drug called an mGluR5 antagonist in humans with fragile X syndrome. The mGluR5 receptors (metabotropic glutamate subtype 5 receptors) perform a variety of functions in the central and peripheral nervous systems. For example, they are involved in learning, memory, anxiety and the perception of pain.

Fragile X syndrome and its associated disorders are the result of a mistake in the number of repeats of three nucleotides on the FMR1 gene on the X chromosome. A normal X chromosome generally has between five and 55 repeats of these nucleotides. Repeats above 200 result in fragile X syndrome. In the absence of the FMR1 gene’s protein product, FMRP, brain development is impaired.

Without FMRP, activation of cell pathways by mGluR5 goes unchecked. It has been theorized that this plays an important role in fragile X syndrome. To examine this hypothesis, earlier studies have used laboratory mice without an active FMR1 gene, but with a reduced amount of mGluR5 protein. The mice showed 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 important in fragile X syndrome, and suggested a path for drug development to treat it.

To test the theory in humans, 12 study participants recruited by Rush and the M.I.N.D. Institute received a single oral dose of fenobam. The study found that in six of the study participants there was a 20 percent improvement in sensory gating, attention and inhibition, through a protocol developed by David Hessel of the M.I.N.D. Institute and of the UC Davis Department of Psychiatry and Behavioral Medicine.

Other study authors include Sarah Coffey of the UC Davis M.I.N.D. Institute and the Department of Pediatrics at UC Davis Medical Center; Crystal Hervey, of the Department of Pediatrics at Rush Medical Center; Andrea Schneider of the UC Davis Department of Psychiatry and Behavioral Medicine and the UC Davis M.I.N.D. Institute; Jennifer Yuhas, of the Department of Psychiatry and Behavioral Sciences at UC Davis; Julie Hutchison and Michael Snape of Neuropharm Ltd.; Michael Tranfaglia of the FRAXA Research Foundation; Danh V. Nguyen of the Department of Public Health Sciences at UC Davis.

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The UC Davis M.I.N.D. Institute, in Sacramento, Calif., was founded in 1998 as a unique interdisciplinary research center where parents, community leaders, researchers, clinicians and volunteers collaborate to study and treat autism and other neurodevelopmental disorders. More information about the institute is available on the Web at <http://www.ucdmc.ucdavis.edu/mindinstitute/>.