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Clinical trials aim to help boys with fragile X syndrome

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In some ways, Samuel is like many other little boys. He likes swimming, riding in his grandfather's boat, and playing games on the family's Wii. His face lights up when he sees an image of Lightning McQueen from the movie Cars.

However, learning to talk has been slow for him. Now six years old, Samuel learned to count before he could say "Mommy." His parents noticed something was different early in his development.

"He still learns and grows. He just does those things differently," says Samuel's father, John McKinnon.

For one thing, Samuel tends to flap his arms when excited—one reason that his pediatrician first suspected he might have a type of autism spectrum disorder. In 2008, Samuel was diagnosed with fragile X syndrome, the most common inherited form of intellectual disability and also the most common single-gene cause of autism.

His parents threw themselves into supporting him. They taught him sign language to help his communication skills. His mother, Wendy McKinnon, puts many miles on her car getting him to appointments with several therapists—speech, physical, and occupational as well as a specialist in applied behavior analysis.

Now, Samuel is one of the youngest participants in a clinical study testing arbaclofen, a drug that scientists think could compensate for the

changes in the brain caused by fragile X syndrome. His parents say they are keeping their expectations in check.

"Our family and our therapists are telling us the same thing—not to put too much hope in the trial," says Wendy McKinnon. "We're trying hard not to read too much into it if Samuel says a new word or plays more with other kids."

Targeting molecules

The majority of children with fragile X syndrome have some kind of developmental delay, and their behavior varies widely. Behavior problems can include hyperactivity, inattentiveness, aggression, or social withdrawal. The average age of diagnosis is approximately 3-1/2 years.

In 1991, a team led by Stephen Warren, Emory's chair of human genetics, discovered the gene whose inactivation is responsible for fragile X. Two decades later, a potential strategy for treating fragile X based on Warren's landmark work is reaching a critical phase in human clinical trials. Three pharmaceutical companies—Seaside Therapeutics, Hoffmann-LaRoche, and Novartis—are sponsoring multi-center studies of drug therapies that take the same biochemical approach, and Emory is participating in all three.

While some children with fragile X syndrome take antidepressants or attention-focusing stimulants, the medications in these studies are the first treatments that scientists think can specifically target the molecular changes caused by fragile X inactivation. Previously tested with promising results in adults with fragile X syndrome, the drugs are now being tested in children and teens with the disorder—some as young as five. Clinicians expect these studies to answer important questions about whether learning and behavior deficits can improve with the medications.

"It's exciting that the research has gotten to this point," says Jeannie Visootsak, principal investigator for the fragile X clinical trials at Emory. "Childhood is when the behavioral problems typically start, so earlier intervention could potentially make more of a difference."

Provided by Emory University