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Lost Boys Found

SCOTT LAFEE - 13 September 2017

At one-and-a-half years old, “Timmy” knew his colors, shapes and numbers in English, Spanish and Farsi. He could put together puzzles faster than anyone else his age. He was a joyous and sociable boy. But by three years old, Timmy had seemingly disappeared, diagnosed with autism.

By the time he was 11, Timmy spoke only “in short two- and three-word sentences,” said his mother. “He was prone to echoing other people’s words and getting hyper, running to and fro in any social setting.”

The story is a common one for children diagnosed with autism spectrum disorder (ASD), a condition estimated to affect 1 in 68 children. But what happened next with Timmy is uncommon and, perhaps, the promise of a better future. Earlier this year, UC San Diego School of Medicine researchers conducted a phase I/II safety trial investigating the effects on autism of a 100-year-old drug called suramin. In Timmy and four other boys ages 5-14, a single low dose of suramin resulted in nearly immediate improvements in core symptoms of autism.

Timmy became calmer. He spoke in complete sentences and remembered his numbers. He began eating new foods and joked with his therapist. Yet while his cognitive and behavioral improvements expanded over several weeks, they gradually declined and disappeared as the suramin dose wore off.

“It shows that all of these kids are capable of doing great things and they are sort of locked into their own bodies. And this is a drug that can unlock that,” said Timmy’s mother. “That’s sort of where we are as parents. You know your child is in there.”

The study was a coup for Dr. Robert K. Naviaux, who has spent the last 10 years pursuing a new unifying theory for the cause and treatment of autism. Naviaux has long sought a drug that could test his hypothesis that ASD is fundamentally associated with a treatable metabolic syndrome.

“Metabolism is the language that the brain, gut and immune system use to communicate,” says Naviaux. “These systems are linked. You can’t change one without changing the others. Each of these systems works differently in autism, but more specifically, the communication between these systems is changed.”

Naviaux suggests the key to autism lies within the cell danger response (CDR), a natural and universal cellular reaction to injury or metabolic stress. CDR prompts cells to barricade themselves from both perceived threats and neighbors. But CDR can get stuck, and if it happens during early childhood development, Naviaux believes autism is the result. “When cells stop talking to each other,” he says, “children stop talking.”

Suramin appears to temper the CDR, blocking alarm signals so that cells return to a normal state and resume normal functions and development. “We have tried every new treatment out there for over 10 years,” said the mother of a 14-year-old trial participant. “Nothing has come close to all the changes in language and social interaction that we saw after suramin. We saw our son advance almost three years in development in just six weeks after suramin. We want to see now if a few doses of suramin over a few months might help him even more.”

That’s Naviaux’s plan. While the initial trial results were encouraging, longer and larger trials with multiple doses will be necessary to further prove his theory. Naviaux is seeking donors to fund that effort, as all of his suramin research thus far has been supported by philanthropy.

“Additional trials may prove suramin is not the answer,” Naviaux says. “Its effects might be limited or not self-sustaining, or side effects could emerge.” But Naviaux believes his work can open eyes and possibilities, not just that suramin might be effective, but that ASD is not immutable.

“Right now, developmental psychologists are taught that autism is permanent—our research suggests otherwise.”

Cellular War

To test his theory that autism is a metabolic and potentially treatable condition, Dr. Robert Naviaux with the School of Medicine conducted trials of suramin, a sort of "cellular peacekeeper."

"When cells are injured, stressed or perceive a threat, the cell danger response is triggered. Cells behave like countries at war," Naviaux explains. "They harden their borders. They don't trust their neighbors. But without constant communication with the outside, cells begin to function differently."

These different cell behaviors include spewing a molecule called adenosine triphosphate or ATP. ATP outside a cell acts as a danger signal, telling other cells to shift resources toward defense, or calling them to war. An ATP imbalance can then cause cells' nuclei to alter gene expression, which can result in developmental dysfunction. When this occurs in childhood, Naviaux believes, that may mean autism.

Suramin tells cells to stop spewing ATP. "It silences the siren," says Naviaux, "signaling the cellular war is over, the danger has passed and cells can return to 'peacetime' jobs like normal neurodevelopment, growth and healing."

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