



Making connections. Psychiatrist Matthew Siegel at work with children in protective headgear.

PSYCHIATRIC RESEARCH

Severe Autism, Often Slighted, Now Targeted for Study

Greg Kapothanasis is 20 years old but has the cognitive ability of a preschool child—and he can't speak. Two years ago, after his school bus ride lengthened to nearly an hour, the 6-foot-tall teenager became increasingly aggressive, lashing out at people, hitting himself on the head, and moving around unpredictably. "The noise really set him off," recalls his mother, Irene. "He just started bouncing off the walls."

Greg has severe autism. His parents had him admitted to Spring Harbor Hospital, in Westbrook, Maine, which specializes in stabilizing such children with acute behavioral problems. Child psychiatrist Matthew Siegel determined that Greg also suffered from an anxiety disorder that triggered his aggression. Clinicians who don't work with severe autism might not know how to assess the mindset of a nonverbal adolescent with the IQ of a toddler. But Siegel knew what to look for.

Siegel's expertise is now being used on a bigger scale. This month, with \$1.2 million in grant funding from the Simons Foundation and the Nancy Lurie Marks Family Foundation, Siegel is spearheading a new consortium dedicated to studying severe autism. Together, the six consortium members—all in-patient facilities staffed by psychiatrists and behavioral specialists—will admit roughly 1000 autistic children in acute behavioral distress per year. By joining forces, Siegel says, "we can maintain a more permanent research infrastructure to accelerate the pace of discovery."

Children who can speak, stay still, and cooperate during testing are overrepre-

sented in studies of autism, Siegel says. Low-functioning children—up to half of all autistic children, by some estimates—have far greater care needs, "but we know virtually nothing about them," says Helen Tager-Flusberg, a psychologist and developmental scientist at Boston University School of Medicine. "If we really want to understand the disorder, we need to look at both ends of the spectrum," Siegel says.

No matter where they land on the spectrum, children with autism share the same core features: trouble relating to and interacting with other people; restricted interests in just a few objects or activities; and a tendency to engage in repetitive behaviors, such as hand-flapping or humming. What sets severely autistic children apart is their lack of verbal and intellectual abilities. These children speak only a few sentences, if at all. According to Siegel, the ability to communicate by age 5 is the number one predictor of later ability to function. "So verbal ability is a hugely important factor," he says. "But we are almost nowhere in our understanding of the difference" between children who can speak and those who can't. This is a key challenge for the consortium.

Characterizing the psychiatric problems that can accompany severe autism is another objective. According to Robin Gabriels, director of the Neuropsychiatric Special Care unit at Children's Hospital Colorado in Aurora (a consortium member), it's often these "comorbidities"—like Greg's anxiety—that set off a child's most troubling behaviors.

Research shows that a third or more of

high-functioning autistic children suffer from anxiety, obsessive-compulsive disorder, attention deficits, or major depression, and Siegel thinks these problems may be even more prevalent in severe autism. Psychiatrists normally diagnose these conditions by having a patient respond to questions. Because severely autistic children can't do that, "we have to rely on careful observation" and "translate the [standard] criteria through an autism lens," Siegel says. He aims to develop methods that others can use.

The high-volume, hospital-based nature of the project will give researchers an unprecedented opportunity to observe behaviors such as self-injury, a common problem in this group. Some children hit themselves on the head and break blood vessels, or bite themselves and develop infections. Gabriels says that self-injury can stem from a need for attention and control or a need for sensory stimulation. Siegel adds that lack of verbal ability might also be a factor, but this needs study.

Eventually, the consortium plans to examine genetic differences in the autistic population. The largest genetic database in autism so far—the Simons Simplex Collection at Rutgers University's Cell and DNA Repository in Piscataway, New Jersey, and funded by the Simons Foundation—has samples collected from over 2700 families. But it deliberately excluded nonverbal children with a mental age below 18 months. "What we want now is a better understanding of this severely affected population, both from the genetic and clinical perspective," says Simons Foundation Senior Scientist Alan Packer.

Genetic insights should allow scientists to define subgroups of affected children. "We need to connect the dots between genetic aberrations and clinical presentations," Siegel says. "Do kids with autism that don't speak have a different set of genes than those who do?" Ultimately, he thinks this approach could lead to better-targeted treatments.

Bryan King, director of the Autism Center at Seattle Children's Hospital in Washington, says the new research agenda is long overdue. "This slice of the autistic population is both the most complicated and the most understudied," he says.

Meanwhile, Greg is doing much better, his mother reports. "When we admitted him, he was going 150 miles per hour," she says. "Now he's doing great. He likes to go grocery shopping."

—CHARLES SCHMIDT

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