

NEWS

Sibling studies reveal early signs of autism

BY VIRGINIA HUGHES

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Baby talk: By the end of their first year, infants who go on to develop autism already show distinct features of the disorder.

In the spring of 2003, when he was 4 months old, Cara Collier's son wouldn't look her in the eye. At 9 months of age, he still wasn't responding to his name. At 18 months, he began biting and banging his head. Six months later, when he was diagnosed with autism, Collier immediately signed up for research studies at the **Center for Autism & Related Disabilities** at the University of Miami.

Scientists there told Collier that they also study the siblings of children with autism. "They told me if I ever chose to have more kids, that they'd keep an eye on them for me," she recalls. "The earlier you notice the signs, the sooner you can start treating them with therapy."

When Collier got pregnant with her daughter in 2006, she enrolled in a sibling study. Through her pregnancy, the researchers tracked her health, diet and how the pregnancy differed from her first.

After Collier's daughter was born, researchers periodically tested the infant's developing speech patterns, eye gazes and the electrical activity of her brain, and watched her playing with her mother, with others and with toys.

Autism has a strong genetic component. Having a sibling with autism significantly increases the

risk of the disorder, although estimates vary between 3¹ and 20 percent.

In the past few years, dozens of research groups have begun studying the younger siblings ? or baby sibs, as they are dubbed ? of children with autism to try to pin down the genetic, developmental and behavioral trajectory of autism and its subtypes. Recognizing symptoms early could also lead to earlier diagnoses and intervention.

"We don't know yet the constellation of subtle factors that come together to produce autistic symptoms," says Daniel Messinger, a developmental psychologist at the Miami center. "But we're all betting that studying the siblings will give us a handle on that."

Researchers hope, for instance, to address what factors lead to the milder Asperger syndrome rather than to autism, and why the language abilities of some kids with autism seem to regress.

"In order to truly understand what these things mean, we have to be able to map them onto the stages of early development," says clinical psychologist **Ami Klin** of the **Yale Child Study Center**. "We haven't made any watershed discoveries yet, but we are asking better questions now than we were even two years ago."

Early onset:

Because autism is a developmental disorder, experts say the brain changes that lead to the disease probably occur early in life. "The first two years of life can be seen as the Holy Grail of this condition," says Klin.

Unfortunately, parents and pediatricians typically don't notice autism's telltale symptoms ? such as an inability to tell imaginative stories or an aversion to playing in groups ? until a child is old enough to talk and interact with others. "Until about 10 years ago, autism clinics like ours would almost never see children below the age of 3," says Klin.

In most cases, experts have had to rely on the parents' memories or on home videos of the children to track how the children behaved before their diagnosis. The retrospective analyses from these "birthday party studies," suggested that the symptoms of autism manifest much earlier than age 3.

"Even at the first birthday party, we found clear signs that distinguish the kids who go on to develop autism," says developmental psychologist **Geraldine Dawson**, whose lab at the University of Washington in Seattle was among the first to use the videotapes.

Dawson's group found that at 12 months of age, children with autism make little eye contact with others, and don't turn their head when their name is called. They tend to pay more attention to objects than to people and don't make pointing or 'showing' gestures².

Still, these video studies are flawed. Celebratory parties involve lots of people, movement and noise ? far from an ideal setting for observing everyday behavior. "Parents will try to get the [children] to smile for the camera or tickle them," Klin notes. "They're forced interactions."

Learning from sibs:

The first large study characterizing families of "psychotic" children was published in 1960³ but baby sib studies in autism didn't begin in earnest until 40 years later, when autism research was more focused on the role of genes.

About five years ago, **Lonnie Zwaigenbaum**, then at the McMaster Children's Hospital in Ontario, designed a diagnostic test called the Autism Observation Scale for Infants. Using this tool, Zwaigenbaum measured the temperament, eye contact and cognitive and language development of 150 baby sibs.

His findings, published in 2005 in the *International Journal of Developmental Neuroscience*⁴ were similar to Dawson's. By 1 year of age, baby sibs who go on to develop autism already exhibit very specific behaviors ? such as not smiling, not reacting to social stimulation, not tracking faces with their eyes and fixating on particular objects ? compared with normally developing baby sibs.

"I don't think any of us anticipated that there would be so many changes happening in the first year of life," says Zwaigenbaum, now a developmental pediatrician at the University of Alberta.

Based on his research, Zwaigenbaum estimates that between 15 and 20 percent of baby sibs develop autism ? much higher than the highest published estimate of 8 percent⁵.

"Those rates were published in the mid 1980s," Zwaigenbaum says, when autism rates in the general population were underestimated and before most diagnostic subtypes for autism existed. "So it's not unreasonable to be a bit skeptical of those old recurrence rates."

On the other hand, the higher estimates may also be inaccurate because they are based on a self-selecting group of parents who may not represent the general population.

Subtle differences:

The ideal study would observe a child with autism beginning at birth and at regular intervals thereafter.

The first wave of those studies aimed to characterize autism's behavioral symptoms⁶. Newer studies are more focused on early genetic and neurobiological indicators of the disorder.

For instance, using head circumference data and brain imaging techniques, **Joseph Piven's** group

at the University of North Carolina has found that children with autism show unusually rapid brain growth, most likely just before the end of their first year⁷.

"What's remarkable about that is the overlap between that and the finding from the Zwaigenbaum baby sibs study," Piven says. "They're both showing that the onset of autistic symptoms occurs in the latter part of the first year of life."

Piven's initial studies relied on retrospective analysis of medical records, but in a baby sib study launched in December, Piven is tracking the brain size of 500 baby sibs as they grow. The **four-site study** is following the sibs at 6, 12 and 24 months with both a behavioral assessment and an MRI scan.

Once that study is complete, "We'll be able to correlate what's going on in brain development with what's happening in language and social behaviors," Zwaigenbaum says. "We'll be able to see what's happening rather than just infer things."

Piven notes that in all of the baby sibs research so far, no extreme differences have been found between autistic kids and their siblings in the first year. "There are some differences at 6 months, and maybe even some at 3 months, but they're not the defining features of autism," he says.

These subtle differences may mean that early therapeutic intervention could steer a child's brain development away from full-fledged autism.

"It's a humbling experience when you realize that despite all of your research experience, it can be very difficult to make distinctions at these early stages," Zwaigenbaum says. "It raises the possibility that maybe the disability of autism isn't firmly established at that point ? that there may be greater potential to put kids back on track."

For parents of these high-risk baby sibs, early testing at least brings peace of mind.

Coller's daughter is now 15 months old and developing normally. "It's a very comfortable feeling to know that these doctors know your child is at high risk for autism," Coller says. "And that they know exactly what to look for."

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