Researchers define characteristics, treatment options for XXYY syndrome

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Researchers at the UC Davis M.I.N.D. Institute and The Children's Hospital in Denver have conducted the largest study to date describing the medical and psychological characteristics of a rare genetic disorder in which males have two "X" and two "Y" chromosomes, rather than the normal one of each. The study, published in the June 15, 2008, issue of the *American Journal of Medical Genetics Part A,* also offers treatment recommendations for men and boys with the disorder.

"We found that there are a variety of behaviors, learning disabilities and emotional problems that are unique to patients with XXYY syndrome that may be better addressed with more targeted therapies," said Randi Hagerman, medical director of the M.I.N.D. Institute and senior author of the study. "Our research is important because it provides an accurate picture of what patients are experiencing that can help physicians who treat patients with the disorder."

XXYY syndrome is a sex chromosome anomaly that is thought to occur in about one in 18,000 males in the general population. Boys with XXYY syndrome usually come to the attention of physicians because of unique facial features, developmental delays, late puberty and behavioral problems. It was once thought to be a variant of Klinefelter syndrome, in which males have one extra X chromosome. While the two disorders are similar in some ways, clinicians have become increasingly aware that they are distinct in some significant ways. The current study set out to identify the unique features of patients with XXYY for the purposes of informing the medical community and improving treatment approaches.

"Until now, physicians have had to search the medical literature to patch together a treatment plan mostly based on information on Klinefelter syndrome," said Nicole Tartaglia, an assistant professor of pediatrics at the University of Colorado Denver School of Medicine who was a fellow at the M.I.N.D. Institute when the study was conducted. "As a result, people with XXYY weren't being screened for the specific medical problems associated with their disorder. They weren't receiving therapies or medications for the behavioral and neurodevelopmental issues that are more profound for them. And they weren't receiving the types of community services that can help them live independent lives. Our research is an important resource for families and practitioners."

For the current study, Tartaglia and Hagerman examined 95 males with XXYY syndrome between the ages of one and 55 years of age. Among their medical findings were that 19.4 percent had cardiac abnormalities such as congenital heart defects and mitral valve prolapse, 87.6 percent had dental problems such as severe dental caries and malocclusion, 15 percent had seizures and 59.8 percent had asthma or other respiratory issues. Intention tremor became more common with age and was present in 71 percent of study participants over 20 years old. 45.7 percent who underwent brain MRIs showed abnormal white matter that may explain some learning difficulties.

Psychologically, the researchers found that 72.2 percent had attention-deficit/hyperactivity disorder and up to 28.3 percent had autism spectrum disorders. In the previous literature, mental retardation was the norm. This study, however, found that only 29.1 percent had IQ scores within the mental retardation range. Learning disabilities were the more common cognitive impairments, affecting 70.9 percent of study participants.

"Life skills are more of a struggle for these males, and they may need different medications, a broader array of behavioral therapies and more

intensive community support than those with Klinefelter syndrome," Tartaglia said.

Lack of comprehensive information about the syndrome is what drove the current study. For years, parents of boys with XXYY syndrome supported each other over the Internet, sharing stories of heartbreak and frustration. While their sons suffered everything from heart defects to learning disabilities, they could only point doctors and teachers to a 1960s scientific paper that first identified the condition along with a few outdated notes on its outcomes.

"We knew we needed a more complete description," said Renee Beauregard, of Aurora, Col., whose 26-year-old son, Kyle, was diagnosed with XXYY syndrome at age 10. "We were tired of having our families running around the country looking for answers from people who didn't have them," said Beauregard, who is also a co-author on the study.

In 2003, Beauregard and other parents turned their frustration into advocacy and established the XXYY Project to support families.

"The more we talked, the more we realized our boys had things in common that were not addressed in the literature," said Beauregard, the project's director. "We had to do something."

The parents had their children take part in the study, and they flew Tartaglia to the United Kingdom so that she could include XXYY boys living there in the research as well.

Now, with more concrete answers, parents like Beauregard and children like Kyle can find some peace of mind.

"Kyle knows that people don't understand XXYY and therefore don't

understand him as a person, she said. "The study helps the world know why he is like he is. It validates what he knows about himself and what we know about him. When he can't follow directions, it's not because he's stupid."

Source: University of California - Davis