

**EVERYDAY ETHICS**

## The XYY Story as a Cautionary Tale: How Scientific Misinformation and Common Biases Can Negatively Impact Lives and Opinions

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### ABSTRACT

In recent decades, huge strides have been made in the field of genetics. Genomic analysis technology has enabled scientists to explore how genetics affect every aspect of human life and development. Genetic testing is poised to be at the forefront of contemporary medicine. Parents often grapple with the correlation of their child's genetic mutations and serious diseases. At a time when misinformation spreads through the popular press like wildfire, we are recounting the XYY story as a cautionary tale to highlight the importance of scientists speaking up and standing against the misuse of genetic information.

The visualization of human chromosomes in the 1950s opened an important era of discovery in biomedical sciences. Scientists Marthe Gautier and Jérôme Lejeune were the first to identify the extra chromosome that caused trisomy 21, better known as Down Syndrome.<sup>1</sup> Karyotype analysis, or the analysis of human chromosomes, then led to the discovery of hundreds of other chromosomal variations that have proven to be essential for the diagnosis of genetic diseases. Although advances in genetics have led to effective treatments, they have also been used to draw lasting damaging and false connections between genetic profiles and human behavior. Karyotype analysis eventually led the research group of geneticist Patricia Jacobs<sup>2</sup> to ask whether an extra Y chromosome correlated with more aggressive behavior and criminality.

The research for the answer to this question had many unforeseen consequences. The stigma that developed around XYY syndrome caused a cascade of unfortunate issues. In this article, we recount cases of inequality, premature pregnancy termination, and misinformation in the health care system regarding the XYY chromosome diagnosis. We showcase this example to make readers aware of how current cases of chromosomal variation could create bias in medical diagnoses.

### REVIEW

XYY syndrome (also known as 47, XYY, and Jacobs syndrome) is a genetic condition in which individuals born with male sex, who typically have one X and one Y chromosome, have an extra Y chromosome. The syndrome, which occurs in 1 out of every 1,000 individuals born with male sex, is shown by recent data to have effects on fertility and an increased possibility for an atypical neurocognitive phenotype. Although research is limited, there is evidence of slightly altered or slowed development of reproductive organs in people with XYY syndrome. Studies have also shown that supernumerary sex chromosome syndromes, including XYY, place children at an increased risk to show symptoms of Autism Spectrum Disorder.<sup>3</sup>

The Jacobs team examined the karyotypes of inmates at the former State Hospital for the Criminally Insane in Carstairs, Scotland. In 1965, Jacobs et al<sup>2</sup> published an article in *Nature* observing that 3.5% of inmates of the Edinburgh institution carried an extra Y chromosome. Although Jacobs et al<sup>2</sup> concluded that the individuals with the XYY karyotype were likely not very different from the non-XYY prisoners, the article was poorly titled "Aggressive Behavior, Mental Sub-normality and the XYY Males." The title apparently reflected what they were asking, not what they found, but it nevertheless suggested an association between the XYY genotype and criminality. The title opened the flood gates for popular news outlets to disseminate the information implied by the title as established scientific evidence. *Science Digest* and *Time* magazine reported on Jacobs et al's<sup>2</sup> research using headlines like "Chromosomes and Crime."<sup>4</sup> Although this was not the case, such stories in the press led to public concern about people carrying an extra Y chromosome. Bias against people with XYY was also perpetuated through various news stories. In 1966, 8 nurses in Chicago were murdered by Richard Speck. Because of miscommunication between a journalist and scientist, news spread attributing Speck's homicidal behavior to his having the XYY mutation, even when blood tests proved otherwise.<sup>5</sup>

In the years following the original publication, Jacobs' claims of the link between XYY and criminality were further disproved. It was revealed that many individuals in the study done by Jacobs et al<sup>2</sup> who had the XYY genotype had committed petty crimes against property, not people.<sup>6</sup> Additionally, subsequent studies analyzing the proportion of individuals with XYY in criminal institutions never came close to the 3.5% that Jacobs et al found in their original study. Despite these findings, XYY testing and the stigmatization of individuals with an extra Y chromosome continued.

During President Nixon's time in office, his personal psychiatrist, adviser, and confidante, Dr Hutschneker, suggested that all 7- to 8-year-olds in underserved or poorer areas be karyotyped for homicidal or violent tendencies. If these children were an XYY match, Hutschneker suggested that they be placed in interventional institutions.<sup>5</sup> This practice perpetuated an extremely dangerous stereotype of criminalizing people from marginalized groups, rather than attributing their behavior to their childhood, surroundings, or the racist biases that incriminate them.

In 1973, a group of young researchers and doctors at Harvard Medical School in Boston, including Dr Jonathan Beckwith, learned that a researcher at Boston Lying-In Hospital was seeking pregnant women who might allow the study of their newborns to determine which, if any, male-sexed newborns had XYY syndrome. The consent form did not disclose that the chromosome analysis was being supported by the Crime and Delinquency division of the National Institute of Mental Health.<sup>7</sup> If the newborns had the XYY karyotype, Dr Stanley Walzer, who was leading the study, would contact the parents to inform them and offer his help and observation as the children grew up. The skeptical group of Harvard scientists, including author Beckwith, had seen the dangers in the XYY screening as a self-fulfilling prophecy and proposed that Harvard Medical School's standing committee on medical research evaluate the XYY screening protocol and potentially suspend it, if warranted.<sup>7</sup> After the Harvard committee initially stated that the study should continue, the critics of the project approached the Children's Defense Fund in Boston, which in turn contacted the Massachusetts Attorney General and the study was finally halted. The publicity from this halted study resulted in the cessation of similar studies elsewhere as addressed by Hamerton in his presidential address to the American Society for Human Genetics.<sup>8</sup>

The *New York Times* covered the change in sentiment about the XYY karyotype in an article titled "A Chromosome Link to Crime is Doubted"<sup>9</sup> in 1976. The article mentioned that the original conclusion that individuals with XYY were more likely to be criminals was false. Rather, it was more likely that the slight increase in criminality was

typically caused by a lower intelligence quotient and Autism Spectrum Disorder associated with the chromosomal mutation.<sup>9</sup> The paper also interviewed Dr Witkin, an American psychologist who pioneered developments in perception as it related to learning. Dr Witkin suggested that society would not gain anything from identifying individuals with XYY and placing them into intervention. Rather, he recommended that the educational and cognitive deficiencies that were associated with the XYY karyotype should be dealt with when problems arise.<sup>10</sup>

In 1982, 17 years after the publication of her original paper,<sup>2</sup> Dr Jacobs retracted her initial statements saying, "In retrospect, I should not have used the words 'aggressive behavior' in the title of my paper and should not have described the institution as a place for 'the treatment of individuals with dangerous, violent or criminal propensities.'"<sup>11</sup> Still, the XYY narrative persisted for many years in the media, with various episodes of *Law and Order* and the film *Alien 3* featuring an antagonist with the XYY karyotype. A Hastings Center conference report in 1980 queried various geneticists and scientists on their opinion and experience with the XYY controversy. Saleem Shah, an Indian-American psychologist who worked closely with mental health and the law, noted that when having the XYY karyotype made somebody a criminal, he "started to receive calls from attorneys asking what [he] knew about the extra Y chromosome and its relevance to the legal issue of criminal responsibility."<sup>12</sup>

Despite all the trouble stemming from the initial Jacobs et al<sup>2</sup> XYY study, additional researchers over the past 30 years have sought to link negative behavior to genetics. In 1993, a Dutch group reported that individuals carrying a mutation eliminating the function of a gene for monoamine oxidase A (MAOA) were more likely to exhibit abnormal and sometimes violent behavior.<sup>13</sup> Many of the individuals with this mutation came from the Pacific Islands, and the mutation was named the warrior gene.<sup>14</sup> As in the case of individuals with XYY, the warrior gene was stigmatized, and those with the mutation were classified as aggressive or having violent behavioral tendencies.

In a 2016 publication, a group of researchers in India claimed that the presence of Barr bodies, chromatin structures formed from the condensation of X-chromosomes, was linked to criminality in men. The article entitled "Do the Presence of Barr Bodies in male jail inmates indicate criminality: a pilot study"<sup>15</sup> studied an exceedingly small sample of 100 inmates and concluded that individuals with Barr bodies were likely to become criminals.

Articles with suggestive titles describing studies with faulty experimental procedures pose a great threat to science and society. As in the XYY case, these studies are

overrepresented in the media. Deceptive media coverage leads society to promote false beliefs about various groups and instills fear of people with certain genetic makeups. Minority groups and low-income families or targeted racial and ethnic groups are the first to be marginalized and presumed to have conditions involving behaviors stereotypically associated with these groups.

## CURRENT IMPLICATIONS

In more recent studies, scientists continue to use genetic ancestry to shape societal values. Increasingly, geneticists are working with social and behavioral scientists to connect certain phenotypes in a genetic ancestry to specific behavioral and cognitive outcomes. Recent social and behavioral genetic (SBG) studies have determined that the phenotypes that some scientists say are predictors of one's social, intellectual, or economic outcome in life are no more predictive than family income and geographical location. Jonathan Beckwith once importantly noted that many flawed genetic studies attempt to "explain away problems by genes and distract attention from social conditions that cause problems."<sup>16</sup>

In an article published in "The Ethical Implications of Social and Behavioral Genomics,"<sup>17</sup> the authors caution that if SBG studies analyzing phenotypes are to be conducted, they must be carefully reviewed, evaluated, and sometimes restricted from publication.<sup>17</sup>

Genetic testing has its benefits as well. Genetic testing helps physicians define chromosomal mutations and genetic disorders that may inhibit or alter childhood development, so parents may be prepared and take preemptive steps for their child. It is when this genetic testing is used for purposes other than ensuring the health of an individual or the population, that it becomes a detriment to society.

A world in which a person's every trait can be predicted by their genetic ancestry and makeup is a very dystopian one. Although futuristic science and technology can act as forces of progress, they can just as easily spread information that can be used to alter societal opinions. It is our duty as scientists to speak up against bad science just as Jonathan Beckwith and his colleagues did during the initial XYY study.

In the wake of the COVID-19 pandemic, the problem of misinformation is metastasizing—with more and more retractions from high impact factor journals, the demise of numerous online journals populated with manuscripts generated by paper mills, and the popularization of artificial intelligence (AI)-generated content. Scientists, editors, publishers, and even readers bear an increased responsibility for preventing inaccurate or misleading titles and content from being published and popularized. Preventive measures could include a more thorough vetting of

submissions for publication and soliciting of diverse opinions and expanded use of AI detection software that would prevent the use of computer-generated or modified images and content. Misinformation can spread like wildfire. Therefore, it is essential that scientists consider the broader social context and consequences of misleading, or frankly false, information.

## Acknowledgments

Dr Beckwith has had a long and extremely successful career in the field of genetics and microbiology. In his early career, he led the research group that isolated the first gene from a bacterial chromosome, and his research continued to flourish from there. Mostly notably, outside of his career in scientific research, he is a controversial activist of social justice and civil liberties in the science community. He was an important organizer in the activist organization Science for the People, which fought against inequality and unethical practice in the field of science. He continued his career as the American Cancer Society Research professor of Microbiology and Molecular Genetics at Harvard Medical school.

I (Helena Ebeling) am an undergraduate student at Boston College, with an aspiration for medical school. My interests mainly lie within genetics and scientific communication as technology advances. Working alongside Dr Beckwith and his deep conviction in the importance of communication in the impact of science and society has sparked the same passion in myself.

Dr Beckwith has more recently been struggling with an Alzheimer disease diagnosis. In an effort to keep the words of one of the most brilliant minds alive, he and I drafted this manuscript together as he recounted his efforts in the 1970s to prevent unethical research and shared his opinions on more recent ethical dilemmas. Together, we reviewed articles, studies, and news publications surrounding the controversial case of the XYY karyotype, as well as paralleling current research. Dr Beckwith has been my inspiration as he continues to amaze with his knowledge and dedication to this cause. With this article, I hope that his insight can be passed on and be an inspiration for the future of medicine and research.

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