Why Autism Strikes More Males Than Females

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I have chosen this topic because of my desire to better understand why individuals are affected by autism spectrum disorder (ASD), and more specifically, why more males than females are given the diagnosis. I did an action research project in a school that specifically caters to autistic students in a Midwest suburban area. This school had a number of children with a diagnosis of autism, varying in levels of disability. I was able to observe the characteristics of autism firsthand. While working in the school, I noticed there were a higher number of male students than there were female students, which reflects the higher rate of ASD in males than females nationally. I wondered why there are more males more than females with this diagnosis, as this might help give clues to future diagnosis, social coaching, education, and prevention. What genetic differences could account for this male-female divide? I decided to look into what current research has found.

Students with ASD can have impaired speech, less developed motor skills, difficulties communicating, and sometimes self-harming behavior. They experience many difficulties socially and academically. Socially the students suffer a form of disconnect with their peers because of their communication difficulties. They also avoid recess and playground activities and prefer to spend more time around adults. Children with ASD are often bullied by their peers and treated differently by their teachers (Auger, 2013).

It has long been noticed in the scientific community that autism affects more males than females; there's a 2012 report showing that autism currently affects 18.4 in 1000 male children, and only 4.0 in 1000 female children. This means males are four to five times more likely to be diagnosed with autism (Stacy et al., 2013). We know hundreds of genes behave differently in the brains of people with autism compared with unaffected people (Sanders, 2011). However the reasoning behind this male-female

divide continues to be researched and debated. As child psychiatrist and geneticist the author said, the reason behind this divide is taking longer than any researchers expected and parents and families of individuals with ASD have been patient (Sanders, 2011). The good news is that recent studies have finally been making a small dent to give us clues.

One such study examined how girls' DNA exhibits autism-related genome duplications and deletions. In this study, researchers from Switzerland worked with scientists from the University of Washington School of Medicine. They collected and analyzed DNA samples and sequencing data from people with autism spectrum disorders and other neurodevelopmental disorders. Researchers examined CNVs, or large disruptions in the DNA that often affect several genes. They found that females had, on average, more large deleterious CNVs than males (Hack, 2014). The affected females were actually two to three times more likely to have a deleterious CNV than the affected males.

Then the researchers at this study looked at whether they could see the same trend in point mutations disrupting only a single gene. Females had an excess number of severe mutation events compared with males. They also saw a difference in truncating mutations (SNVs), which produce a shorter or more broken protein. This means females affected by this have more mutations from CNVs and from sequence mutations (Hack, 2014).

The results of genetic study indicate girls are more resistant to genetic causes of autism, which seems to suggest that females can have the same genetic insult as males but not receive an autism diagnosis (Sanders, 2011). The author of the genetic study stated that girls tolerate neurodevelopmental mutations more than boys do. This means that it takes more mutations for girls to show signs of autism or other disorders.

On the DNA study is promising because it found consistent results after examining such a large number of participants. The researchers looked at two populations that were large, including over 9000 males and over 6000 females. All of the individuals had been diagnosed with neurodevelopmental disorders. They also used a large control population (Hack, 2014). With this high number, there is more reliability in the study's results. In the future, it should be good to examine why females have this resistance and talk about how this finding can positively influence diagnosis and treatment of the disorders.

The DNA research could be one clue as to why more boys are diagnosed with ASD. It could also better help diagnose girls who may not show symptoms as easily as boys. With more information coming out regarding specific genetic mutations, there may be a chance in the near future to diagnose ASD earlier on and better specify treatment. This could even be helpful in scientists' work to develop medications and other forms of prevention and treatment.

Another recent study looked at postmortem human brain tissue and did a genome-wide analysis on tissue from 16 brain regions. It included tissue from preconception to adulthood and analyzed sex-based genes together. The study proposed that the higher number of males with autism might be linked to male-specific brain transcriptional modules with the same pathways in ASD. Researchers found that ASD might disturb the suites of genes that fit into sex-specific brain development. They also discussed the role of immune activation in ASD because immune responses had a significant gender dimorphism. Researchers concluded its role in ASD and relation to sex differences is still unclear and more environmental than genetic. However, they said the results suggest that this transcriptional program uses the immune system could make a normal human brain more "male" somehow because of the links with the sex-specific areas. Their results also suggest that sex-specific transcriptional modules could make males more likely to develop neurodevelopmental disorders from problems in these pathways, both from the environment and from inheritance (Ziats & Rennert, 2013).

Because this research (Human Brain Tissue) hasn't been linked to very specific findings yet, it will be important to see more studies examining these points. It will be interesting to see how these immune system components may make a difference when it comes to ASD and then see what the causes of these might be and how it can be reversed. Because the pathways can be susceptible to inherited and environmental aberrations, it will also be interesting to see how these two factors could be used together to make a difference in ASD. With more information regarding environmental factors, parents and teachers could help improve the environment to lessen the effects of the disorder. At this time this is not one of the most promising theories, but it is a possibility to keep in mind while examining studies that have more backing.

Of these recent studies that have more meat to them, several have been based off the extreme male brain (EMB) theory, which was first proposed in 1997. It comes from the Empathizing-Systemizing (E-S) theory. The E-S theory says that, on average, females have more drive to empathize and males have more drive to systemize. One promising study suggests ASD is caused by the extreme male brain. The researchers based this off the evidence that ASD is both neurobiological and genetic, with environmental influences. They also considered that more males are affected than females and that it takes more for females to exhibit the affects of ASD. This theory also reinforces the first study mentioned, with males being more likely to be influenced by genetic mutations (Baron et al., 2011).

Baron's study examined scores for the Empathy Quotient (EQ) and the Systemizing Quotient (SQ). Researchers found that on the EQ, typical females scored higher than typical males who scored higher than those with ASD. On the SQ, individuals with ASD scored higher than typical males, who scored higher than typical females. The study also noted that the amygdala in typical males is usually larger than those in typical females' amygdala. In early development, the amygdala in individuals with autism is even larger than a typical male's. In addition to this, animal studies confirmed that affect of early exposure to androgens (like testosterone) encourages the brain shift in behavior, cognition, brain structure, and function as they relate to sex. There has also been a link in several studies between current androgen dysregulation in individuals with ASD or their relatives (Baron et al., 2011).

If the issue is with improper exposure to androgens, it could be beneficial to figure out how the individuals are receiving the increased exposure so it could be prevented. Another innovation that could be helpful could be the ability to shift the levels of androgens after the exposure. Monitoring the size of a fetus' or infant's amygdala could also be helpful in diagnosing ASD earlier, especially if there is a specific correlation with size and level of ASD.

The study also states that it's widely accepted that fetal testosterone (fT) exposure affects brain development and behavior. Males have a surge in levels of fT between eight and 24 weeks during gestation. This first surge almost reaches the levels human males experience in puberty and is thought to be a major part of brain masculinization. Because of ethical reasons, scientists can't directly manipulate hormone levels in fetuses. However some tests, such as amniocentesis during the second trimester of pregnancy, can

be done at different stages to monitor the levels and the affects on behavior. In addition to this, the researchers stated that increasing levels of fT are linked with more rightward asymmetry in the thickness isthmus in the brain, which is related to language and visuospacial activity. It's known to be an indicator of the differences between males and females through its structure and function (Baron et al., 2011).

In the future, it's possible there will be tests that better help determine hormone and fT levels of the fetus without doing harm. Determining these levels could help in diagnosing ASD and monitoring interaction and behavior. It could be possible in the future to develop methods to increase or decrease hormone levels according to how they correlate with ASD symptoms in males and females. It will be interesting to see how more analysis of the isthmus helps (or doesn't help) in the search for the reason why more males are affected with ASD than females. If the fT levels are changes the structure of the isthmus, perhaps better monitoring those levels will maintain the isthmus. Larger studies will have to be done to determine these relationships.

The X Chromosome Theory is another theory to consider when looking into the genetic reasons that may explain why males are more often affected than females when it comes to ASD. Researchers have already found that mutations in the X chromosome, which contains more genes in the brain than the other chromosomes, are linked to learning difficulties. An X mutation is associated with ASD through Fragile X Syndrome; 46% of males and 16% of females carrying the full mutation also have ASD (Baron et al., 2011).

This theory has some holes in it – most studies that examine the X chromosome in relation to ASD have failed to find regions of interest. Nothing specific has come to light to point clues to how the X chromosome might affect males more than females, though researchers are still trying to do this. In relation, genomic imprinting is of interest. Genomic imprinting is "the process by which genetic effects are influenced by whether the genes are transmitted through the father or the mother". Normally, this wouldn't prove to change anything to do with the sex, but this could happen if imprinting takes affect on the X chromosome (Baron et al., 2011).

One theory was inspired by the findings that the rate of social difficulties vary depending on whether the single X chromosome was inherited from the father or the other. Typical females inherit an X chromosome from both

parents while ales have only one from the mother. The theory is that a gene expressed on the X from the father acts as protection against social issues in people affected by ASD (Baron et al., 2011).

This last theory seems to make sense from what is known about the X chromosome. If the X holds the most genes in the brain, and males only have one X, they don't have as much defense for issues that may arise genetically in the brain. Females could better fight mutations, as mentioned in all above studies, possibly because of their two X chromosomes. This X chromosome theory requires much more research to find more substantial links, but could be useful in diagnosing ASD and other related disorders.

In conclusion, the question as to why more boys are diagnosed with autism than girls has yet to be answered. Fortunately now there are have been many recent studies to ask this question and go deeper into research. There are a lot of different atypical genetic patterns that result in developmental disorders. We can see from these studies that females seems to be more resilient to them, showing less developmental problems even when they have some genetic abnormalities. This was demonstrated in the study by University of Washington, where they discussed the major difference between boys and girls and their resilience to mutations that result in ASD.

To build on that, there are theories related to the extreme male brain theory, where ASD is caused by this. In this case, things that make a brain more "male", like the tendency to systemize of empathize, may be due to overexposure to androgens like testosterone, or greater surges in fT. Similarly, when males have only one X chromosome, from their mother, they may not have the same defenses as females do, with their X chromosome from each parent. This lack of protection in the chromosome that holds the most genes in the brain cause the affects of ASD to be more severe.

The main thing to remember is that the difference between males and females with ASD is caused by genetic vulnerabilities. It's important to continue to study the genetic elements of ASD and how it relates to males and females in order to properly diagnose and treat the disorder, as educators rely on diagnosis and treatment of the disorder to properly teach their students. Being able to know the diagnosis of a child opens doors to managing their behavior, social interactions, and lesson planning. It will be interesting to see how research progresses with this topic as I enter my

teaching career. I hope to be able to utilize the coming research in my own classroom.

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