THE GENETICS OF ASD

After an individual is diagnosed with Autism Spectrum Disorder (ASD), some of the questions that a family may ask include:

- What are the possible causes for ASD?
- Could other family members be at risk for developing ASD?
- What does this mean for future generations?

Genetics and genetic testing may provide some answers to questions like these.

Doctors know that genetics play a role in the development of ASD because scientists have studied ASD in identical twins, in fraternal twins, and in single-birth siblings. Identical twins share nearly all of their genetic information, so it would be expected that both twins would have ASD if there were a genetic cause. Research has shown that when one identical twin has ASD, the other twin also has ASD in 60-90% of the cases. This rate is very high compared to the fraternal twin concordance rate and the rate of ASD recurrence among single-birth brothers and sisters, which are about 20%.

The significant difference in the percentages tells researchers that there is a good chance that ASD is related to something in the genes. However, because identical twins don’t both have ASD in 100% of cases, researchers also know that something else is involved in the development of ASD for many individuals. If one identical twin has ASD and the other twin does not, it is possible that something in the child’s environment or experience may be a factor in the child’s ASD.

Because of this, ASD is considered a complex genetic disorder, involving both genes and environmental factors. Environmental factors refer to anything that a developing child could be exposed to, such as medications during pregnancy or maternal infection. The environmental exposures known to be associated with ASD with prenatal exposure include thalidomide, valproic acid, misoprostol, alcohol (in quantities sufficient to cause Fetal Alcohol syndrome), and rubella.
infection. Environmental factors also refer to things a child might experience. More research is needed to understand the link between the genetic and environmental factors.

For the majority of people with ASD, a specific genetic change causing ASD cannot be identified. A genetic cause of ASD is more likely to be found in those whose life skills are in the lower-functioning range or those who have other significant medical issues. Currently, a genetic cause can be identified in about 20% of cases. These genetic causes can be chromosomal abnormalities, changes in single genes, or copy number variants (deletions and duplications). Genetic testing is available to detect these types of genetic changes.

<table>
<thead>
<tr>
<th>Genetic Cause</th>
<th>% of ASD</th>
<th>Type of Genetic Testing</th>
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<tbody>
<tr>
<td>Chromosomal Abnormalities</td>
<td>Up to 5%</td>
<td>Chromosome Analysis or Karyotype</td>
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<tr>
<td>Single Genes</td>
<td>Up to 5%</td>
<td>Testing of individual genes like the Fragile X gene</td>
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<tr>
<td>Copy Number Variants (CNVs)</td>
<td>Up to 11%</td>
<td>Chromosomal Microarray Analysis (CMA)</td>
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It is likely that more research will discover that the percentage of individuals with
ASD with a clear genetic cause is greater than 20%, but research so far has not been able to accurately characterize those causes. Possible causes still to be identified include very rare single gene mutations that have not yet been discovered and specific combinations of several factors, including variations in genes that occur in society at large, but which cause ASD only when occurring in certain combinations.

Researchers now believe that the number of genes that puts a person at risk for ASD is between 500 and 1000. Any one individual with ASD might have just one or a few risk genes, but these genes can affect the brain in similar ways. One reason that ASD is so heterogeneous in its presentation (“if you’ve seen one person with autism, you’ve seen one person with autism…”) is that different individuals with ASD may share to a greater or lesser extent different underlying causal mechanisms. Scientists are eager to learn more about these biological foundations because a clearer picture of what causes ASD will allow for the development of specific biological treatments which could be very powerful and effective.

Related Articles:

- ASD and Other Genetic Conditions
- Clinical Genetics Evaluations
- Genetic Information Non-Discrimination Act
- What Causes Autism?

Additional Resources:

- Working Up Autism: The Practical Role of Medical Genetics
- SFARI gene

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