Although there has been much progress in studying and understanding autism, scientists still do not understand what causes autism. Scientists and clinicians have believed for awhile that there is a common cause for the three characteristics seen in people with autism: (1) difficulty with social interactions, (2) difficulty communicating with others, and (3) restricted and repetitive behavior. There is increasing suspicion among researchers that autism does not have a single cause. In this review article, the authors looked at scientific evidence on changes in the brain of people with autism, genetic causes, and environmental causes. The authors were looking for evidence about how these factors might work together to explain how and why autism develops in certain people but not others. They also thought a combination of factors might better explain the different behaviors and intellectual abilities we see in people with “Autism Spectrum Disorders (ASD).”

This study is a review article that evaluated published research and clinical articles on autism. The authors reviewed articles that studied or described genetic causes of autism, changes in the brain of people with autism (neuro-anatomy), and environmental factors. Environmental factors are things that people are exposed to that may cause a negative reaction in their body.
Results
(What did the Researchers find?)

Broad Autism Phenotype
When this article was published in 2003, there was a lot of research showing that not all people with ASD were affected the same way in their social ability, communication, and repetitive behavior. There was also beginning bio-medical research that showed that people with ASD had different brain sizes and structures. This type of research looks at what is called ASD “phenotype.”

A “phenotype” is the word clinicians and researchers use to describe any characteristic or trait of an organism or person. In the picture to the right, you can see nine eyes. They all look like a human eye, but each has a different color and shape. The color and shape of the eye for each human being is one of their unique characteristics – part of their phenotype. Just like the color of someone’s eyes, humans have other common features which together, make them unique. A person’s cheekbones might stand out like a model, or be flat. Their nose may be large, small, flat or tall, crooked or straight.

Their mouth may be large or small, with lips which are narrow and thin or full and large. Their ears may stick out or be flat against the head, tiny, big, or average in size.

In addition to how people look, all human beings vary in how their bodies work. The average person can typically stand, walk, run, use their hands to do many things, but one may be a fast runner, another an artist or a javelin thrower.

Similarly, people vary in many different types of intelligence – cognitive, artistic, creativity, social and emotional intelligence. Some people are good at math, science, or engineering, some are good at computers, others are gifted at talking, and others are good with people.

Finally, we are learning more about differences in people’s health, behavioral, and developmental characteristics, which also is a way to describe groups of people we are studying.

Although research shows that humans vary on many characteristics, scientists have found that when you study a specific characteristic in hundreds, sometimes thousands of people, the differences you see across people fall within certain limits, often called “within normal limits.” For example, all people have two eyes and their eyes are separated by a certain distance. This “normal” distance is between 45 mm and 70 mm. If the distance between a person’s eyes are 35 mm then this would be considered unusually small. If the distance between a person’s eyes is 85 mm then this would be considered unusually large. Being
“outside of normal limits” does not necessarily mean that something is wrong, but a clinician would take a second look if a child had a number of unusual characteristics that are “outside of normal limits.”

Much of the bio-medical and genetics research on autism documents the characteristics of people with autism or their phenotype – how they look and how they behave. Understanding the characteristics of people with Autism (how similar and different people with Autism are) helps researchers understand whether we can expect people with autism to look and act very much the same and explain why people with autism look and act differently. More and more, researchers are looking at differences in the brain and nervous system of people with Autism when compared to people who do not have Autism. What the brain looks like and which parts of the brain appear to be affected when a person has ASD is also a part of the phenotype of people with autism, which scientists are trying to understand.

Research articles describing how a person with Autism looks and behaves began in 1943, by a child psychiatrist at Johns Hopkins University in Maryland, Dr. Leo Kanner. Since then, many articles have been written to describe how children with autism are different than other children (their phenotype). For many years, the term Autistic Disorder referred to a developmental disorder which occurs by 3 years of age. General characteristics of children with Autistic Disorder included (1) impairments in social ability, (2) language impairments and (3) restricted patterns of interests which may involve repetitive behaviors. Articles on “Asperger’s Syndrome” were first published in 1980 and described a broader group of children who had “autistic-like” features. These children did not have severe problems in these three areas. Autistic Disorder and Asperger’s Syndrome are now grouped under the term “autism spectrum disorders” or ASD. Children with this diagnosis have a broad range of characteristics, from mild to severe. They may have different combinations of problems. Researchers agree that there is no single description of people with ASD. They also believe there is evidence that suggests there are multiple causes of autism.
Evidence That There are “Sub-groups” of People with Autism

In their review, the authors described the results of articles that showed evidence that there are sub-groups of people with ASD. For example, they described many studies which report that there are many more males with ASD than females with ASD. See Figure 1.

When sub-groups of people with ASD are studied, the number of males to females changes. Figure 2 shows a study of the ratio of males to females for people with ASD whose head size were (1) smaller than normal (microcephaly), (2) normal size, and (3) larger than normal (macrocephaly). This study found that there were more males than females with a normal or larger than normal head size. About the same number of males and females had head sizes which were smaller than normal. If the subjects with ASD had head sizes smaller than normal, the number of males and females was about the same.

In another study, the researchers grouped subjects into 3 groups: people with severe ASD, those with moderate ASD (most people with ASD), and people who are high-functioning. See Figure 3. When they looked at the number of males and females in each of these groups, they found that there were about the same number of males and females in the group with severe ASD and those that were high-functioning. However, males were not more common than females in the middle group, which is where most people with ASD fall.

If there were only one cause of autism, then the number of males and females with SD would not change if their head sizes were different or their disability was mild, moderate, or severe. The results of these types of studies are some of the reasons why researchers think there are many causes of ASD and ASD is a very complex disorder.
Developmental Regression and Environmental Factors

The authors reviewed the articles which described two groups of children with ASD. Some children were diagnosed because their development was different than other children their age without autism. Their speech and social interaction was different from the beginning (birth). In other cases, about 30-50% of children who were diagnosed with ASD lost skills or an ability they had before (in early childhood). This usually occurred when the child was between 18-24 months old. Scientists call this “developmental regression,” because children lose a function they had before. Many parents reported this happened after a stressful event for the child, such as an infection, trauma, operation, or vaccination. When a child loses a function, researchers do studies to try and explain why this happened. Either it was a coincidence or perhaps the child was exposed to something in the environment that hurt him or her. The MMR vaccination is one example of an “environmental” factor which some people thought caused ASD. The authors pointed out that the studies they reviewed suggest that the MMR vaccine does not cause ASD. However, they stated that we need to better understand if there might be a gene or set of genes that might make a child more likely to develop ASD if they are exposed to an environmental factor when the child’s brain is young and developing.

Studies of the Brain in People with ASD

A number of studies have looked at the brains of people with ASD to see if there is evidence that there are changes in the brain that will help us understand what causes ASD. These brain studies might also explain what parts of the brain are affected when a person has ASD. Some studies have looked at the brains of people with ASD who have died. Most studies look at clinical measures of the size of the brain. One clinical measure that is used by clinicians and researchers is “head circumference.” This is a measurement of the largest part of the head which is from the middle of the forehead all the way around. When babies are born, the skull or bone protecting the brain is not closed all the way. This is so there is enough room for the brain to grow. The soft spot in the skull closes in a child by the time they turn 2 years old. Head circumference can tell us about the development of the brain. A smaller than normal head circumference, called microcephaly, may mean the brain did not develop fully. A larger than normal head circumference may mean the brain is developing differently than the average child. Published articles state that the head circumference of people with ASD is much larger than...
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Other researchers have studied the brain of people with ASD using imaging techniques—pictures of the brain. There is new evidence that the brain of children with ASD grows faster than normal in the early years. Then the growth of the brain is much slower than normal afterwards. This makes researchers believe that the child’s body is not able to control fast the brain grows. Researchers have also found that the brain of a child with ASD uses more energy than other children without ASD. This evidence might mean that the child’s brain might not be able to control how much energy it is using. This might be a result of the same problem with controlling the brain’s growth.

Genetics and Autism

There has been a great deal of research trying to find a genetic cause or multiple genetic causes of ASD. Researchers are pretty sure that genes are part of the complex causes of ASD. Genetic studies have found sites on a large number of chromosomes that have a positive link to ASD. This means that ASD is not a result of a specific chromosome like Down Syndrome (Trisomy 21) or a specific genetic abnormality. Currently, it is believed that several genes interact with one another or with environmental factors to produce the various clinical characteristics (phenotype) of ASD. There is also a belief that genetic causes create a “susceptibility” to developing ASD. The gene makes it more likely that a person will develop ASD, but it may need some environmental injury or trauma, at the right time of development of the child’s brain. If these 3 things do not happen at the right time, the child may not develop ASD or the ASD might be very mild. Uncovering all of this is complicated. Researchers suggest this is where future research should focus.
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What does this mean for my child and my family?

Families should be careful when learning about the causes of ASD from just one research study. Families should look at review articles like this—article where the authors review many studies. This kind of article will give families a better understanding of what we know and don’t know right now. If you are concerned about how genes or the environment have played a role in your child’s autism, talk with your child’s doctor. If you are worried that you will have another child with ASD, talk with your obstetrician. You can take this brief with you and show it to your doctor.

Glossary of Terms

**Genetics/Genes** – The body’s genetic code contain the instructions for how the body will look, grow and function. A gene is the smallest thing that can be biologically passed on from one generation to another.

**Environmental** – “Environment” refers to anything surrounding an object or person. What is in a person’s environment (what is around them) can enter the body through the air (breathe into the lungs), through the skin, through our eyes and ears. Things that we put into our bodies (things we eat, drink) and medications we take or are given are also considered part of the environment. Things in the environment are called Environmental factors. Many things in our environment make us healthy (such as food, clean water, sunlight and clean air). Some things in our environment can make us sick.

**Phenotype** – The term clinicians and researchers use for any characteristic or trait of an organism. The phenotype for children with ASD includes how they look (the size of their heads), how they behave, GI problems, allergy, and other medical problems that are considered to be common to people with ASD.

**Regression** – To return to a previous state of being. Developmental Regression means the child goes backward to an earlier stage of development. For example, a toddler who is drinking from a cup and then wants to drink from a bottle again.

**Head Circumference** – A measurement around the largest part of the head—usually about the middle of the forehead all the way around the head. Most doctors measure head circumference when the baby is born and at each medical visit. The doctor will also measure height and weight. We have statistics on what is normal head size and what is small and large for age.

**Toxins** – Materials or chemicals that have a bad effect on the body or poisons.
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