Autism Insights

EDITORIAL

Autism Etiology: Genes and the Environment

A.J. Russo

Health Research Institute/Pfeiffer Treatment Center, Warrenville, IL 60555, USA. Email: ajrusso@hriptc.org

Epigenetics involves the relationship between genes and the environment, specifically, covalent modifications occurring in DNA and associated chromatin, allowing cells to maintain distinct and different characteristics, despite containing the same genetic material. Etiology of diseases of epigenetic origin involve the interaction between genes and the environment, where the environment has a distinct role in determining these modifications.

Recently, researchers have focused on finding a genetic cause for Autism Spectrum Disorders (ASDs). After all, in studies where autism was found in identical twins, both have autism more than 60 percent of the time, depending on the criteria used.[1] When fraternal twins have autism, both have autism up to 6 percent of the time.[2] Family histories show that the chances of someone with autism having a brother or sister who also has autism is between 2 percent and 8 percent[3]—much higher than in the general population. Also, some of the autism-like symptoms, such as delays in language development, occur more often in parents and adult brothers and sisters of people with autism than in members of families without autism,[4] and in approximately 5 percent of autism cases, another single-gene disorder, chromosome disorder, or developmental disorder is also present.[3]

So, why not focus on genes. All the billions spent on the Human Genome Project resulting in new technology and a database unparalleled in the history of medical research, available to anyone who wants to use it.

Although some analysis suggests that as many as 15 genes might be involved in ASDs,[5] the strongest evidence points to areas on: Chromosome 2[5–8]—which has the "homeobox" or HOX genes, that control growth and development very early in life. Chromosome 7[9–12,14]—which houses the AUTS1 gene, related to speech and language disorders, the MET gene which signals neocortical and cerebellar growth and maturation, immune function, and gastrointestinal repair, and the Reelin (RELN) gene. Chromosome 5[15] contains the CDH9 and CDH10 genes responsible for the synthesis of cadherin proteins. Chromosome 13[5,12]—In one study, 35 percent of families tested showed linkage for chromosome 13. Chromosome 15—Genetic errors on this chromosome cause Angelman syndrome and Prader-Willi syndrome. Both share behavioral symptoms with autism, and cytogenetic errors on chromosome 15 occur in up to 4 percent of patients with autism.[12] Chromosome 16—A genetic error on this chromosome causes tuberous sclerosis, a disorder that shares many symptoms with autism, including seizures. So, regions on this chromosome may be responsible for the similar behavioral characteristics seen in autism.[5] Chromosome 17[12,13]—Missing or disrupted genes on this chromosome can cause problems, such as galactosemia, a metabolic disorder that, if left untreated, can result in mental retardation.

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Chromosome 17 also contains the GABA pathway genes and the gene for the serotonin transporter synthesis, which allows nerve cells to collect serotonin, which, in turn, is involved in emotions and helps nerve cells communicate. Problems with the serotonin transporter have also been shown to be associated with obsessive-compulsive disorder. Two disorders, which share symptoms with autism, Fragile X syndrome and Rett syndrome, are caused by genes on the X chromosome.

But, genes by themselves don't explain the complex etiology of ASD. Involvement of epigenetic regulatory mechanisms in the pathogenesis of ASD has been suggested because of the occurrence of ASD in patients with disorders arising from environmentally associated mutations (fragile X syndrome) and the involvement of key epigenetic regulatory factors (Rett syndrome). Moreover, the most common recurrent cytogenetic abnormalities in ASD involve maternally derived duplications of the imprinted domain on chromosome 15q11–13.[16] Parent of origin effects on sharing and linkage to imprinted regions on chromosomes 15q and 7q suggest that these regions warrant specific examination from an epigenetic perspective, particularly because these modifications do not change the primary genomic sequence, allowing environmentally effected alleles to evade detection using standard screening strategies.[16]

And, after all, in studies where autism was found in both identical twins, both have autism more than 60 percent of the time. It is likely that epigenetic influences explain why some of the 40 percent don't develop ASD.

With regard to getting a better handle on the elusive etiology of ASD, and the potential relationship between genetics and the environment, one can't help but sense the pull and tug. Geneticists tugging on available research funding. Environmentalists pulling on already highly invested research. As we try to zero in on the pathophysiology of autism, before the rope breaks, it behooves researchers to work together, because in all likelihood, both genes and epigenetic factors will ultimately help explain the dozen or so diseases we now categorize as Autism Spectrum Disorders.

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