


Familial Autism Genes

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THE CAUSES OF AUTISM ARE

Although the etiology of autism is not known, firstly in 1943, American psychiatrist Leo Kanner defined Autism as language use disorders, inability to use the language of communication, excessive dependence, over-dependence against sameness, repetitive behaviors, life-long appearance as a chronic disorder, with changes in the appearance and severity of symptoms with age and maturation.^[1] He stated that no difference was observed between the social classes in terms of the risk of autism.^[2] According to the psychoanalytic approach, which is the popular trend of the period, by Kanner, it was defined only in relation to inadequate or incorrect parental attitudes, regardless of their biological basis. After Kanner's explanations, it has been revealed that as the researches on autism increase, autism may be due to biological reasons. Recent studies have focused on the genetic factors of the disease. The incidence of autism in the families and relatives of autistic children is more than 10-20% higher than the normal children, the rate of autism among siblings is 60-90%, and the prevalence of one or more of the autism children in the family and relatives of autistic children. They are meaningful differences that can prove the findings that it is an inherited disease.

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ABSTRACT

Autism is a common developmental disorder resulting from a lack or failure of different cognitive skills such as social interaction, communication and language disorders. In addition, stereotyped behaviors, limited activity and limited interests are observed in people with autism. An autistic person between 0-3 years shows these deficient, inadequate and different aspects. Autistic disorder is diagnosed according to DSM-IV criterias. The incidence is four times higher in boys than in girls. It is a lifelong disorder that cannot be cured completely. The incidence is around 1.7% in society. Although the etiology of autism is unknown, many studies have shown that genetic factor plays a major role. The rate of autism in the sibling of an individual with autism is between 10-20%. This rate is well above the prevalence in society. Many studies conducted with the families of individuals with autism showed symptoms of autism characterized by problems in communication skills, introversion, language and speech problems in family members. In this review, familial autism genes will be discussed and the effects of heredity on autism will be discussed.

Keywords: Autism genes, autism spectrum disorders, autism, chromosomal abnormalities, etiology of autism, genetic transmission.

BIOLOGICAL CAUSES

In studies related to the causes of autism, it has been reported that exposure to thalidomide, especially valproic acid, anticonvulsants, some viral infections and various birth complications are associated with the development of autism.^[3] In addition, it is emphasized that the psychological stress factors encountered by the mother in the prenatal period are associated with the development of ASD.^[4] In imaging studies, some of the children with autism had features of macrocephaly, abnormal increase in cortical white matter, and abnormal growth characteristics in limbic structures such as frontal lobe, temporal lobe, amygdala.^[5] These structures are regions that have an important role in social relations, communication and motor skills that show deterioration in autism.^[6]

In addition, in functional MR studies, hypoactivation^[7,8] and impaired activity of mirror neurons were detected in the fusiform facial region in individuals with autism.^[9] However, none of these findings are specific for Autism Spectrum Disorder (ASD).^[6] The fact that autism can be seen with diseases of genetic origin, the high concordance seen in monozygotic twins and the high risk of disease occurring in siblings reveal the importance of hereditary factors in the etiology of the disease. In twin studies, it has been reported that the concordant rates in single twin twins are between 60% and 90%, while the concordance is between 0-10% in twin identical twins.^[7] Among siblings, it has been shown that 2-7% of co-diseases.^[10] In general, it is observed that genetic factors in autism are responsible for more than 90% of the occurrence of the disease.^[11]

GENES KNOWN TO BE ASSOCIATED WITH AUTISM

Chromosome 2NRXN1, SCN7AChromosome 3GAT1, OXTR, CNTN3, SLC9A9, DIA1Chromosome 7FOXP2, WNT2, RELN, HOXA1, HOXB1, MET, EN2Chromosome 11HRASChromosome 15GABRB3, GABRA5, GABRG3, UBE3A, ATP10CChromosome 175-HTTChromosome 22SHANK3Chromosome XMeCP2, NLGN3, NLGN4, SLC9A6, FMR1.

Genetic research on autism; The first studies initiated to identify chromosomal regions and loci that may cause autism are in the form of connection and relationship studies.^[12]

Although many genes and candidate genes related to autism were found, the major gene could not be detected. Significant results were obtained in 7 chromosome regions related to autism: 2, 3, 7, 11, 15, 17, X chromosomes. In addition, other candidate genes that are thought to cause autism are also being studied. The presence of many genes responsible for social interaction, language, communication and emotions indicates that there may be problems in more than one gene. With the development of technology, it will be possible to evaluate these genes and candidate genes together, and it will be possible to make more comments about the etiology of autism.

SAMPLE CASE REPORT

There are no case reports or studies regarding the risk of co-illness in separate triplets in autistic disorder and other ASDs.^[13] When studies conducted

on twin twins are examined, it is seen that the fear of autism is between 0-10% in these cases. In siblings, the co-morbidity rates are between 2-7%, similar to twins.^[14] Given the findings obtained from twins and siblings, the risk of co-illness among siblings is high compared to the general population, although all three siblings are unlikely to have coincidental illness. The occurrence of co-illness in our cases may have resulted from the fact that genetic factors and environmental factors are effective independently or by interacting with each other. Although no family history of common developmental disorders is described other than these cases, the co-illness observed in the presented cases may be related to the higher genetic susceptibility to autism in some families and the higher risk of spouse illness among siblings in these families. The fact that the presence of families with frequent autism spectrum disorders in family studies also supports this view.^[15] In addition, it was observed that non-autistic siblings had more functional losses such as language, communication, and learning disorders compared to the control group.^[16] It is claimed that genetic factors and family history are more effective in girls. In their study, Ritvo et al. Found 2 times more ASD in boys with ASD siblings than boys. Although ASD is seen four times more frequently in boys than in girls, it can be thought that two of our cases are gender-matched.^[17] Genetic diseases are detected in 10-15% of patients with ASD. The most commonly known are cytogenetic abnormalities such as fragile X (3%), tuberous sclerosis (2%), maternal duplication (2%) of 15q1-q13 (16%) deletion and duplication (1%).^[18] But none of them are specific for ASD. Especially in the 2000s, there was a change in the known genetic views about autism. Today, it is suggested that many genes, from which the common disease-common gene model is not correct for autism, are effective in the phenotype of the disease from mild to moderate level.^[19] In studies, the relationship between autism and the 9th and 10th regions of the street was found to be significant.^[20] Cadherin's neuronal activity is a known molecule. The presence of synaptic functions of the genes that cause fragile X and Rett syndrome also led to the conversion of attention to synaptic dysfunction in terms of the etiology of ASD. Today, the most accepted model in autism development suggested by genetic and neurobiological evidence is that the model has a genetic-based synaptic maturation and connectivity problem.^[6]

Despite all these developments, a single gene that could explain autism is not found yet, except for diseases that can be detected by some chromosomal

and molecular tests. However, studies show that autism is the result of single nucleotide polymorphism, copy number difference, mutations in some target genes, epigenetic interactions (i.e. changes in the gene's nucleotide sequence that have changed function and changes that can be passed on to next generations by mitosis and/or meiosis) and environmental contribution. Each of these factors that mentioned contributes to the formation of autism, but we will be able to better understand the genetic mechanisms that lead to the autism picture through technological advances in gene analysis systems.^[21]

As a result, autism is currently an incurable disease affecting the individual's social interaction, communication, language and intellectual skills based on his limited cognitive skills. Although the cause of the disease can not be explained for a single reason, the fact that it is seen significantly higher in siblings and especially in single twins reveals the effect of genetics related to chromosomal abnormalities. Genes that cause this disease that affect different cognitive skills continue to be explained with more meaningful data day by day with the recent studies and technological developments. In the light of these developments, the importance of genetic causes is emphasized for the differential diagnosis of the disease. This disease, which can not be treated today, will enable the development of methods to reduce symptoms after the biological factors become more evident with new developments.

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