Gene duplications may play a role in developmental disorders with autism-like characteristics

childhood disability LINK

Summary

It is now possible to analyze an individual's chromosomes with extremely high resolution, making it possible to detect deletions or duplications of tiny regions that are undetectable by conventional chromosome visualization techniques. These minute alterations change the number of copies of specific genes that an individual has, and many have been reported in cases of developmental disorders. This study shows that a small region of chromosome 2, about the size of seven genes, is duplicated in two individuals displaying developmental delay (DD), intellectual disability (ID), and other autistic features, while it is not duplicated in individuals without disabilities.

About the study

This study examined the chromosomes and gene expression levels of two young adolescents displaying DD, ID, and other autism characteristics. In both cases, the children had unrelated parents without disabilities and had tested normally for several other disorders. Array comparative genomic hybridization (Array CGH), also known as chromosome microarray analysis (CMA), was used to detect submicroscopic deletions and duplications. Both subjects displayed a similar microduplication between 2q23.1 and 2q23.2. In both subjects, the duplicated region included the genes MBD5 and EPC2; increased expression of these genes was confirmed by quantitative Real-Time PCR (qRT-PCR). More than 8427 control individuals lacked this duplication, as did large populations of individuals lacking disabilities assessed in other projects (one individual in the external control population did, however, display a microduplication).

What families should know

This microduplication is rare, but parents should be aware of it, as it may provide insight into a child's condition when conventional chromosome visualization and other tests show normal results. The children with the microduplication in this study displayed a delay in the

development of skills such as walking and talking and deficient communication as well as distinct facial features. In addition, one child exhibited social indiscretion and aggression.

What practitioners should know

Microduplications or microdeletions may exist even in patients with normal karyotypes, and the gene copy number variations that they introduce may play an explanatory role in a patient's autism like characteristics. These tiny variations of just 1.5-2Mb of DNA can be detected using modern, high resolution chromosome analysis and gene copy number quantification.

Reference

Chung, B., Mullegama, S., Marshall, C., Anath, L., Weksberg, R., Dupuis, L., et al (2012). Severe intellectual disability and autistic features associated with microduplication 2q23.1. European Journal of Human Genetics, 20(4): 398–403. Advance online publication. doi:10.1038/ejhg.2011.199.

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