# Recurrent genetic deletion linked to autism

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Loss of a small portion of chromosome 16, known as 16p11.2, is significantly associated with autism report researchers from the University of Chicago Medical Center, the University of Illinois at Chicago, and the Roswell Park Cancer Institute in an article, published Dec. 21, 2007, online by the journal *Human Molecular Genetics*.

Although this genetic "microdeletion" occurred in only four out of 712 subjects with autism (0.6%), it is the second most common recurrent genomic disorder associated with autism, which affects about one out of 160 children in the United States.

"We suspect that 16p11.2 microdeletions are a risk factor for autism spectrum disorders generally and may cause mild autism in some families," said study author Susan Christian, PhD, associate professor of human genetics at the University of Chicago. "By disturbing the network of affected genes, this loss of selected genes may underlie the development of autism."

The deletion results in the loss of about 25 known genes. "Twelve of those genes appear to be part of a single genetic network that includes genes involved in cell-to-cell signaling and interaction," said first author Ravinesh A. Kumar, PhD. postdoctoral scientist in human genetics at the University of Chicago, "At least three of the deleted genes are primarily expressed in the brain and are thought to influence behavior," he added, "which makes them very promising candidates for autism."

The authors suspect the lost or damaged genes may also be involved in

other cognitive, language and social impairments.

To find genes linked to autism, the researchers scanned the entire genomes of 180 subjects with autism searching for submicroscopic pieces of DNA that were either lost or mistakenly duplicated in patients diagnosed with autism. They first found that two out of those 180 (1.1%) had a deletion in region 16p11.2, on the short arm of chromosome 16. None of the 372 control subjects had the same deletion.

To confirm that result, the researchers screened DNA from an additional 532 subjects with autism. They found two additional subjects with the same deletion (0.4%), which was seen in none of the 465 controls. Combining the two samples produced a total prevalence of 16p11.2 deletions of 0.6 percent.

The 16p11.2 region is flanked on both sides by bands of segmental duplications, short strings of nearly identical DNA that predispose to the loss, shuffling or amplification of this region during genetic recombination. "Many human diseases are caused by these types of chromosomal rearrangements, however, this is the first recurrent microdeletion in autism too small to be seen under a microscope," said Christian.

The most common known genetic cause of autism, linked to about one to three percent of cases, is a much larger duplication of part of chromosome 15, involving about a dozen genes. The chromosome 15 abnormality is associated with autism as well as intellectual disability (www.idic15.org). The chromosome 16 deletion, by contrast, is not consistently associated with intellectual disability.

"Although this only explains about one-half of one percent of autism," said co-author William Dobyns, professor of human genetics and pediatrics at the University of Chicago, "it provides the best clues yet for

finding the specific genetic changes that lead to the disease. This is a small region with a limited number of genes, including several strong candidates, each of which merits a closer look. The next step is to find the specific gene or genes involved. There may be one gene within that deletion that is at the core of the problem."

Source: University of Chicago