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Developmental delay could stem from nicotinic receptor deletion

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The loss of a gene through deletion of genetic material on chromosome 15 is associated with significant abnormalities in learning and behavior, said a consortium of researchers led by Baylor College of Medicine in a report that appears online today in the journal *Nature Genetics*.

"This research goes about 95 percent of the way to pinning these problems in a specific group of individuals to this gene," said Dr. Arthur L. Beaudet, chair of molecular and human genetics at BCM. He believes that the deletion will be identified in other people with behavioral problems as well as schizophrenia, developmental delay and epilepsy. The gene's role in schizophrenia has been under study for some time.

Previously, a larger deletion containing more genes had been reported in people with the same constellation of disorders. In this work, Beaudet, Dr. Pawel Stankiewicz, assistant professor of molecular and human genetics at BCM, and colleagues found that a smaller deletion of genetic material - the whole of the gene in question, CHRNA7, and a part of another - was associated with similar problems in 10 members of four families.

"We scanned the genome of about 10,000 people to find this rare but important defect," said Stankiewicz.

"This gene encodes a subunit of a nicotinic receptor," said Beaudet. "It is a gene that mediates the response to nicotine via a receptor whose normal ligand is acetylcholine." The gene encodes a protein called an ion

channel, which allows ions to flow in and out of neurons in the brain. Defects in ion channels have previously been associated with forms of epilepsy or seizure disorder.

"If insufficient expression of the nicotinic receptor causes most or all of the problems associated with deletions in this particular area of chromosome 15, then it offers a target for drug treatment," said Stankiewicz. One such drug mentioned in the paper is Chantix, a medicine now used in smoking cessation efforts.

In this study, an international group of researchers identified 10 people from four unrelated families with the same deletion in the chromosome. The area deleted encompasses all of CHRNA7, which encodes a whole subunit of the nicotinic receptor.

Nine of the 10 subjects had developmental delay and/or mental retardation. Four of the 10 had seizure disorders or an abnormal electroencephalogram (EEG).

In two of the families studied, the patients had inherited the deletion from a parent. In one family, researchers found the same deletion in the patient's mother, two siblings, maternal aunt and maternal grandmother. Both the patient's mother and her sister had mental retardation and epilepsy. His both siblings had developmental delay. The patient had severe mental retardation and obesity and mild facial dysmorphism.

A second patient with impaired growth and severe developmental delay inherited her deletion from her mother, who had normal intelligence but had suffered from epilepsy from childhood.

Source: Baylor College of Medicine (news : web)