MedicalXpress

The gene family linked to brain evolution is implicated in severity of autism symptoms

March 21 2014

The same gene family that may have helped the human brain become larger and more complex than in any other animal also is linked to the severity of autism, according to new research from the University of Colorado Anschutz Medical Campus.

The gene family is made up of over 270 copies of a segment of DNA called DUF1220. DUF1220 codes for a protein domain – a specific functionally important segment within a protein. The more copies of a specific DUF1220 subtype a person with autism has, the more severe the symptoms, according to a paper published in the *PLoS Genetics*.

This association of increasing copy number (dosage) of a gene-coding segment of DNA with increasing severity of autism is a first and suggests a focus for future research into the condition Autism Spectrum Disorder (ASD). ASD is a common behaviorally defined condition whose symptoms can vary widely – that is why the word "spectrum" is part of the name. One federal study showed that ASD affects one in 88 children.

"Previously, we linked increasing DUF1220 dosage with the evolutionary expansion of the human brain," says James Sikela, PhD, a professor in the Department of Biochemistry and Molecular Genetics, University of Colorado School of Medicine. Sikela is the corresponding author of the study that was just published.

"One of the most well-established characteristics of autism is an

abnormally rapid brain growth that occurs over the first few years of life. That feature fits very well with our previous work linking more copies of DUF1220 with increasing brain size. This suggests that more copies of DUF1220 may be helpful in certain situations but harmful in others."

The research team found that not only was DUF1220 linked to severity of autism overall, they found that as DUF1220 copy number increased, the severity of each of three main symptoms of the disorder—social deficits, communicative impairments and repetitive behaviors – became progressively worse.

In 2012, Sikela was the lead scientist of a multi-university team whose research established the link between DUF1220 and the rapid evolutionary expansion of the human brain. The work also implicated DUF1220 copy number in brain size both in normal populations as well as in microcephaly and macrocephaly (diseases involving brain size abnormalities).

The first author of the autism study, Jack Davis, PhD, who contributed to the project while a postdoctoral fellow in the Sikela lab, has a son with autism and thus had a very personal motivation to seek out the genetic factors that cause autism.

The research by Davis, Sikela and colleagues at the Anschutz campus in Aurora, Colo., focused on the presence of DUF1220 in 170 people with autism.

Strikingly, Davis says, DUF1220 is as common in people who do not have ASD as in people who do. So the link with severity is only in people who have the disorder.

"Something else is at work here, a contributing factor that is needed for

ASD to manifest itself," Davis says. "We were only able to look at one of the six different subtypes of DUF1220 in this study, so we are eager to look at whether the other subtypes are playing a role in ASD."

Because of the high number of copies of DUF1220 in the human genome, the domain has been difficult to measure. As Sikela says, "To our knowledge DUF1220 copy number has not been directly examined in previous studies of the genetics of autism and other complex human diseases .So the linking of DUF1220 with ASD is also confirmation that there are key parts of the human genome that are still unexamined but are important to human disease."

Provided by University of Colorado Denver