Most Autism Cases Tied to New Mutations Not Inherited from Parents

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Most cases of autism are related to the presence of new mutations in the child not inherited from the parents, according to a new study at the University of Washington (UW) School of Medicine.

The findings, published in the journal *Cell*, show that these new mutations occur in both coding and non-coding regions of the genome. Coding regions contain genes that code for proteins, while "non-coding" regions regulate gene activity, but do not contain genes.

"We are excited by these early findings because they suggest that multiple new mutations in a child, both coding and non-coding, are important to understanding the genetics of the disease," said study leader Evan Eichler, UW professor of genome sciences.

Some forms of autism appear to run in families, but most cases occur in families with no history of the disorder. Known as simplex autism, these spontaneous cases are thought to occur from new mutations that first appear when the the parents' sperm or eggs form.

These newly formed (de novo) mutations appear in the child's genome, but not in either parent's genome. They are also unlikely to occur in the affected child's siblings.

For the study, researchers used a huge genomic database created by the Simons Foundation Autism Research Initiative. They compared the genomes of 516 individuals who had simplex autism with the genomes of their parents and one sibling who was not affected by the disorder.

In this way, the researchers hoped to find new mutations that were more likely to appear in the affected child and were more likely to be linked to an increased risk of developing autism.

In most previous studies, researchers had only compared mutations in the small portion of the genome that includes the instructions for the synthesis of proteins. This coding region contains genes. The new study compared almost the entire genomes of the study participants, including non-coding regions that do not include genes.

These "non-coding" regions still play a vital role in regulating protein production by turning genes on and off and dialing their activity up or down.

The researchers found that mutations that appeared in non-coding regions of the genomes tend to occur in areas that influence gene activity in neurons in the brain's striatum, a structure believed to play a role in some of autism behaviors. Typically, the striatum coordinates planning, reward perception, motivation, and other cognitive functions.

Mutations were also found in regions of the genome that influence genes for embryonic stem cell development and fetal brain development.

Overall, very few of the new mutations were needed to increase the odds of having autism. In fact, the risk rose with as few as two of these newly appearing

mutations.

To better understand the role these mutations in the non-coding regions play when it comes to autism risk, it will be necessary to repeat the study with many more sets of parents and their children, said Eichler.

Source: University of Washington Health Sciences/ UW Medicine