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How Much of Cerebral Palsy is Caused by Genetics?

What is this research about?

Cerebral palsy (CP) is the most common cause of physical disability in children. It has many different environmental origins that can damage the fetal or newborn brain, such as a lack of oxygen, stroke (i.e., a blood clot in the brain), trauma, or infection. Genetic causes of CP are usually looked for when no other cause in the environment is found or when the child has features suggestive of a genetic syndrome. Some genetic causes are inherited from parents, while others are new to the child (i.e., *de novo*, meaning new). A specific type of genetic abnormality, called a copy number variation (CNV), has been linked to dozens of human disorders. A CNV is when large chunks of DNA are deleted or copied in excess. We all carry CNVs in our genome, but every once in a while a CNV can hit a critically important gene and based on the gene's function, result in specific clinical outcomes. This study investigated the proportion of children with CP who have large CNVs that are not typically seen in the general population.

What did the researchers do?

In this study, the researchers looked at a random selection of children with CP from the Canadian

What you need to know:

Ten percent of children with CP in this study had variations in their genetic code (called copy number variations). This means that there is likely a mix of both environmental (e.g. prenatal birth stress) and genetics that can cause CP and that wider use of genetic testing in children with CP should be considered.

Cerebral Palsy Registry and did genetic testing on the children along with their parents. DNA was satisfactorily collected from 115 children with CP and both of their parents to look for CNVs. CNVs were called *de novo* when they were not inherited from the child's parents.

What did the researchers find?

In the 115 children examined for genetic CNVs, 11 (10%) had CNVs that were deemed to be a probable or possible cause of CP. Importantly, most of these 11 children also had problems around their birth that may have contributed to CP. Eight of the children had *de novo* CNVs and 3 had extremely rare CNVs that they shared with one of their parents. The children with the largest CNVs that encompassed the largest number of genes had the most severe impairments. CNVs

occasionally provided new information about the child. In one particularly insightful case, a boy with CP was found to have a large CNV that pointed towards an entirely different disorder called Angelman syndrome and as a result, his family received appropriate information about the expected course of his disease.

How can this research be used?

This study shows that CNVs affecting particular genes can cause or be susceptibility factors in CP. For the majority of the families with CNVs, having this genetic information earlier could have helped with understanding, specific treatment, and rehabilitation. In addition, knowing the genetic cause of CP could help with counseling about the risk of having CP in their future children. In light of the high rate of CNVs in children with CP, genetic testing should be a standard part of the comprehensive assessment of any child with CP.

About the Researchers

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Oskoui, M., Gazzellone, M.J., Thiruvahindrapuram, B., Zarrei, M., Andersen, J., Wei, J., Wang, Z., Wintle, R.F., Marshall, C.R., Cohn, R.D., Weksberg, R., Stavropoulos, D.J., Fehlings, D., Shevell, M.I., and Scherer, S.W. (2015). Clinically relevant copy number variations detected in cerebral palsy. *Nature Communications*, 6, pp. 1-7.

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This research summary was written by Jarred Garfinkle, MD.

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