Genetics Study Summary

Thank you to everyone around the world who participated in this research project investigating genetic causes of CP! Our initial findings from this project have been published in Nature Genetics. We wanted to let you know the results of this project at the same time.

BACKGROUND: THE GENOME

First for context, the genome acts as a "blueprint" so your body knows how to make you, you. Like a recipe in a cookbook, your genome is written in the "language" of DNA. DNA itself is made up of four letters: A, T, C and G. Your genome is a total of 3.2 billion letters of your DNA and is unique to you. You have around 20,000 genes in your genome. Scientists and doctors can use technologies such as whole exome sequencing to read your DNA and see if there are any changes that may affect your genes and health.

THE STUDY

This study used whole exome sequencing technology to look at all 20,000+ genes in 250 individuals with CP and their parents from the USA, China and Australia. They were compared with an existing database of 1,789 unaffected siblings of children with autism and their unaffected parents. Potential mutations were then studied in laboratory cells or fly models.

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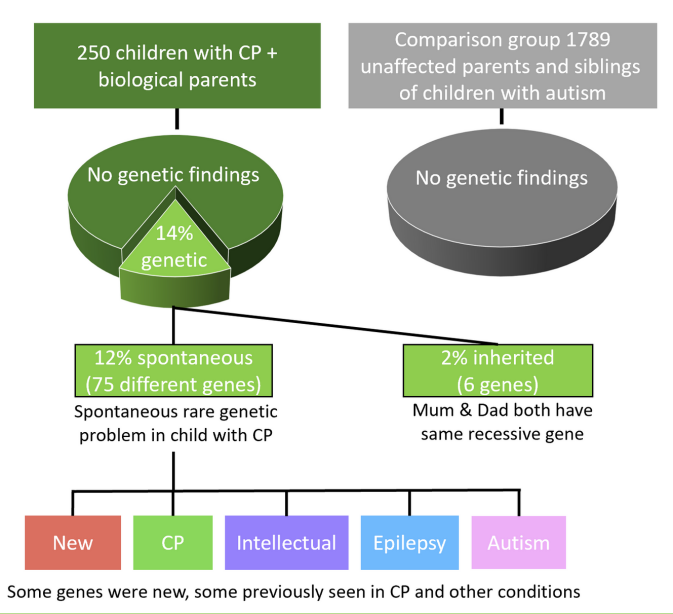
THE RESULTS

The cause of CP was attributed to *de novo* (spontaneous) genetic variants for 12% of the group. These variants were found in a total of 75 genes, mostly involved in brain development and brain wiring. Eight genes were recurrently mutated, meaning that more than one individual had a mutation in these genes. Some of these genes have previously been reported in individuals with CP and some of the genes identified represent new findings. For 2% of the group, genetic variants that were inherited from both parents were identified. These variants were in genes currently associated with Hereditary Spastic Paraplegia. As you may already know, other conditions frequently co-occur with CP. In this study, significant overlap was observed in the genes found in individuals with CP and those reported in individuals with autism spectrum disorders (5%), intellectual disabilities (30%) and epilepsies (10%). As an encouraging aside, as a result of this research, four individuals had changes in their CP management and personalized treatments made available to them.



IN SUMMARY

These findings, made possible through a worldwide collaboration with doctors, scientists, and families such as yours, provide firm evidence that a sizable proportion of CP cases are due to genetic mutations. Our discoveries are already leading to follow-up projects on several continents. Goals of these projects include understanding how genetic changes affect neurodevelopment in cell and animal models, incorporating genetic findings into clinical care for people with CP, and developing new treatments by righting brain wiring. Thank you again to everyone who participated in this study. We will keep you posted on any other findings as they arise and opportunities for you to be involved in further research.

If you have any questions about this please contact Prof Michael Kruer and his team in Phoenix, USA: kruerlab@phoenixchildrens.com

Michael and all the team

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