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Developmental problems: Some exist in the genes

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Everyone is special in their own unique way. From a genetic point of view, no two humans are genetically identical. This means that DNA for each individual contains variants that are more or less comm. on in the overall population.

Some gene variations are actually genetic deletions, where sections of DNA 'code' are missing entirely. These variants are likely to have important effects on gene function and, therefore, likely to contribute to diseases associated with that gene. But what happens when multiple genes are disrupted in a single family?

A large collaborative study led by scientists based in Oxford, Bologna and Utrecht sheds some light on this complicated situation by describing the genomic characterization of a family with two rare microdeletions, in CNTNAP5 and DOCK4. Multiple members of this family were diagnosed with autism, dyslexia, and/or learning or social difficulties.

The genetic analysis revealed that the CNTNAP5 deletion segregated with autism. In contrast, the DOCK4 deletion was present in multiple individuals without autism, but this gene microdeletion co-segregated with reading difficulties.

"This report provides further evidence linking CNTNAP genes with autism, one of the most promising gene families in autism research," commented Dr. John Krystal, Editor of *Biological Psychiatry*, where this research is published. "But it also highlights how complex the connection

between genes and syndromes can be, supporting the importance of DOCK4 for brain development - particularly in circuits involved in reading- but questioning its role in autism."

"This is another example of the emerging theme whereby multiple rare genomic variants within a single family might, in combination, lead to the variable phenotypes associated with autism spectrum disorders," said first author Dr. Alistair Pagnamenta.

Interestingly, CNTNAP5 is closely related to other genes that can influence susceptibility to autism, such as CNTNAP2, which was first identified in 2008. DOCK4 is thought to be involved in the growth and development of nerve cells in the brain. Together, these results may open up new lines of research to help understand mechanisms behind neurological disorders and brain development.

The authors have noted that additional studies, which are needed to confirm these associations, are already underway.

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