Genetic conditions lead to range of overlapping needs in children

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Deletions and duplications of DNA are responsible for wide-ranging developmental difficulties in children, finds a new study by Cardiff University.

Lead author Professor Marianne van den Bree, from Cardiff University's MRC Centre for Neuropsychiatric Genetics and Genomics, said: "We found that psychiatric health as well as development, learning and thinking, motor coordination and sleep quality were affected in children with a range of conditions caused by slight changes in DNA known as copy number variants."

The team looked at these copy number variants (CNVs) in different locations within the genome and found that the developmental outcome for children was broadly the same, regardless of the different genome locations and regardless of whether the variants were deletions or duplications.

Strikingly, comparisons across the different CNV groups indicated there were more similarities than differences in the range of difficulties the children experienced. In particular, the groups experienced similar levels of difficulties with peer relationships, sleep and mood.

First author Dr. Samuel Chawner, from the MRC Centre for Neuropsychiatric Genetics and Genomics, said: "Our findings suggest that all of the different CNVs we observed have similar impacts on the brain and increase the risk of developmental, motor, psychiatric and sleep problems, as well as aspects of intellectual function."

The study, part of the IMAGINE-ID collaboration between Cardiff, UCL and Cambridge Universities, recruited 258 children with CNVs as well as a comparison group of their siblings without these CNVs. With the support of the National Health Service (NHS) the families were recruited from medical genetics clinics within the UK.

The team looked at the impact of 13 different CNVs by examining in detail a range of relevant outcomes, including development, motor and sleep problems, behaviour, IQ , other specific learning, memory and

thinking processes, and risk of psychiatric disorders. The CNVs could be either a deletion or a duplication and they occurred on a number of different chromosomes (1, 2, 9, 15, 16, and 22).

80% of the group with CNVs had at least one psychiatric disorder (14 times increased risk compared to siblings without these CNVs), including ADHD, oppositional defiant disorder (ODD), anxiety disorder and autism spectrum disorder (ASD). Behavioural difficulties were present at home as well as in school.

Professor Jeremy Hall, Director of the Neurosciences & Mental Health Research Institute at Cardiff University, said: "Our findings indicate that children with these CNVs need care that is combined across a range of different medical specialities. This would require changes in the way most services for these patients are currently run. Support and intervention plans for these children also need to be wide-ranging, focusing on their behaviour at home, in school, and with their peers as well as in the clinic."

Professor Michael Owen, Director of the MRC Centre for Neuropsychiatric Genetics and Genomics, added: "Children with these CNVs are not only at high risk of psychiatric disorders and developmental difficulties in childhood, but we know from other work in the Centre that they are also at high risk of adult psychiatric disorders such as schizophrenia and depression. If we can follow these children over time this will give us an opportunity to understand this process and potentially intervene to stop progression."

The study 'Genotype-phenotype relationships in children with Copy Number Variants associated with high neuropsychiatric risk: Findings from the case-control IMAGINE-ID cohort in the United Kingdom' is published in *The Lancet Psychiatry*.

More information: Samuel J.R.A. Chawner et al. Genotype-phenotype relationships in children with Copy Number Variants associated with high neuropsychiatric risk: Findings from the case-control IMAGINE-ID cohort in the United Kingdom, (2019). DOI: 10.1101/535708