MedicalXpress

Adding up autism risks

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The causes of autism and autism spectrum disorder (ASD) are complex, and contain elements of both nature (genes) and the environment. New research published in BioMed Central's open access journal *Molecular Autism* shows that common genetic polymorphisms (genetic variation) can add up to an increased risk of ASD.

The contribution of inheritance and genetic mutation versus environmental factors to the risk of ASD is hotly debated. Most twin studies show the contribution heavily tilted toward inheritance, but the exact amount of involvement of genes in ASD risk is less apparent. This is because, while the impact of rare genetic variations on ASD risk is becoming clear, the role of more common variations, so called single nucleotide polymorphisms (SNP), remains unresolved.

In a vast project involving researchers across the USA, genetic data from families in the Simons Simplex Collection (where one child, but neither parent or any brothers or sisters, have ASD) and the Autism Genome Project (where one or more children were affected), was compared to families from the HealthABC program a cross section of the population).

By analyzing one million of the common variations in each participant's genome, it became clear that, in families where only one child is affected, 40% of the risk of ASD is inherited. In families where more than one child is affected this increased to over 60%. By looking in more detail at the unaffected parents and siblings of children with ASD it appeared that the inherited risk was additive.

Prof Bernie Devlin, from the University of Pittsburgh, explained, "Each of the common variations involved in ASD has little effect on its own, however our results show that they add up. This could explain why, while the parents might each not show any symptoms, their children receive enough of the risk versions to be affected."

Overall these results suggest that there are a large number of common variants each with a very small effect. Prof Devlin continued, "This is a large step forward in our understanding of ASD. The genetic components alone are far more complex than many imagined a decade ago, including the additive effects we have found, rare inherited mutations, and new mutations arising spontaneously before conception."

Editors-in-Chief, Drs. Buxbaum and Baron-Cohen noted that this study represents "An exceptionally important breakthrough in our understanding of autism risk". They also note that, "The interplay between common SNP and rare risk variants could be key to understanding the considerable differences in presentation seen among individuals with an autism spectrum condition".

More information: Common genetic variants, acting additively, are a major source of risk for autism Lambertus Klei, Stephan J Sanders, Michael T Murtha, Vanessa Hus, Jennifer K Lowe, A. Jeremy Willsey, Daniel Moreno-De-Luca, Timothy W Yu, Eric Fombonne, Daniel Geschwind, Dorothy E Grice, David H Ledbetter, Catherine Lord, Shrikant M Mane, Christa Lese Martin, Donna M Martin, Eric M Morrow, Christopher A Walsh, Nadine M Melhem, Pauline Chaste, James S Sutcliffe, Matthew W State, Edwin H Cook Jr, Kathryn Roeder and Bernie Devlin, *Molecular Autism* (in press)

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