Functional impact of global rare copy number variation in autism spectrum disorders

NeuroDevNet researcher, Stephen Scherer, led research that has been recently published in Nature. Network researcher Susan Bryson also helped author the paper.

Abstract: The autism spectrum disorders (ASDs) are a group of conditions characterized by impairments in reciprocal social interaction and communication, and the presence of restricted and repetitive behaviours. Individuals with an ASD vary greatly in cognitive development, which can range from above average to intellectual disability. Although ASDs are known to be highly heritable (~90%), the underlying genetic determinants are still largely unknown. Here we analysed the genome-wide characteristics of rare (<1% frequency) copy number variation in ASD using dense genotyping arrays. When comparing 996 ASD individuals of European ancestry to 1,287 matched controls, cases were found to carry a higher global burden of rare, genic copy number variants (CNVs) (1.19 fold, \( P = 0.012 \)), especially so for loci previously implicated in either ASD and/or intellectual disability (1.69 fold, \( P = 3.4 \times 10^{-4} \)). Among the CNVs there were numerous de novo and inherited events, sometimes in combination in a given family, implicating many novel ASD genes such as SHANK2, SYNGAP1, DLGAP2 and the X-linked DDX53–PTCHD1 locus. We also discovered an enrichment of CNVs disrupting functional gene sets involved in cellular proliferation, projection and motility, and GTPase/Ras signalling. Our results reveal many new genetic and functional targets in ASD that may lead to final connected pathways.