Autism and Neurodegeneration: Linking Copy Number Variations in Genomic Regions of Autism to Neurological Disease

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The human genome comprises millions of nucleotides of DNA packed into chromosomes. Regions of DNA > 1Kbps in size sometimes contain structural variations in the form of insertions/deletions, referred to as copy number variation (CNV). Since genes normally occur in two copies per genome, a variation in gene copy number due to structural variation could lead to chemical imbalances, resulting in disease. Autism Spectrum Disorder (ASD) is a neuro-developmental disorder that causes social, communication, and behavioral challenges. A significant number of children with ASD experience developmental regression characterized by loss of previously acquired skills. Loss of neurological function in ASD as observed in children who have regressed can be explained as neurodegeneration, and a treatment to address this issue is necessary. The goal of this research is to examine ASD subjects for CNVs in chromosomal regions containing genes implicated in neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's disease, to find out whether CNVs in such locations could result in candidate pathways contributing to neurodegeneration in ASD. After statistical tests (P< 10-3), 7 specific genes were identified with CNVs which impacted biological processes relating to memory, learning, and neuronal growth. The effect of the CNVs in terms of deletion/duplication was investigated through the Variant Effect Predictor tool, to assess the neurological implications of transcript ablation/amplification. Results confirmed that variations in gene copy number of the 7 genes affects neurotransmission leading to possible neurodegeneration in ASD. This research further reveals novel treatment options for ASD by incorporating drugs targeting neurotransmission to counter neurodegeneration.