Network-Level Dysregulation of Neurodevelopmental Signaling Pathways in Schizophrenia: A Transcriptomic Analysis

Nkomboni, Ibanathi (School: Dominican Convent High School)

Schizophrenia is a chronic neurodevelopmental disorder. In low-resource settings like Zimbabwe, stigma and limited psychiatric infrastructure delay diagnosis. This study investigated whether schizophrenia stems from network-level dysregulation of neurodevelopmental signaling pathways rather than isolated single-gene defects. An in-silico bioinformatics analysis used human transcriptomic datasets from the NCBI Gene Expression Omnibus (GSE27383, GSE35974, GSE53987, GSE21138, GSE12649), comprising >70 schizophrenia samples and >50 controls. Differential expression was assessed via GEO2R utilizing the limma framework and Benjamini-Hochberg false discovery rate correction (adjusted $p<0.05$). This was followed by protein-protein interaction (STRING) and pathway analysis (Reactome) focusing on the NRG1-ErbB-PI3K/Akt-DISC1 network. Modest but statistically significant, coordinated expression changes were observed across datasets. In GSE27383, PIK3R1 was upregulated (logFC=+0.1294, adjusted p=1.12×10?5), while ERBB2 was downregulated (logFC=-0.3935, adjusted $p<0.05$). Additional pathway-associated genes (GRB10, STAT3, JAK1) also showed significant differential expression (adjusted $p<10?5$). Network analysis revealed dense functional interactions among these genes, supporting systemic pathway-level dysregulation. These findings indicate schizophrenia features distributed transcriptomic alterations across neurodevelopmental networks; however, causal inference is limited by cross-sectional microarray data. This work provides a systems-level framework for future validation, informing hypothesis-driven research for underrepresented populations.

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