A Genomic-Based Investigation of Repetitive Behaviors across Four Neurodevelopmental Disorders Using a Machine Learning Approach

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Although mental illnesses account for 30% of all medical disabilities, the mechanisms behind these disorders are still very poorly understood. A significant spectrum within neurodevelopmental disorders is that of stereotyped and compulsive behaviors, which is associated with the cortico-striatal-thalamic-cortical loop. Among the diseases within this spectrum, the most significant ones are Rett Syndrome, Autism Spectrum Disorders, Tourette's Disorder, and Obsessive-Compulsive Disorder. These neurodevelopmental disorders represent the evolution of repetitive behaviors from simple motor stereotypies to complex limbic compulsions that involve more elaborate interactions between regions of the human brain. In this novel study, our goal is to investigate the spectrum as a whole in order to search for overlaps among risk genes and mechanisms associated with the four disorders. We first performed a systematic review using PubMed. We selected 678 genes related to the risk of developing these diseases. We then used machine learning tools to analyze the interaction between these different genes and the biological processes related to them. By combining the results achieved through several different methods, we were able to develop an evolutionary model describing the progression of the compulsive spectrum. Moreover, we identified two microRNAs, MIR519 and MIR101-1, that regulate genes from all four neurodevelopmental disorders, which is relevant primarily because miRNAs have been found to be ideal targets for drug development; therefore, those miRNAs are possible targets for the treatment of diseases in the spectrum of stereotyped and compulsive behaviors, and may improve the lives of individuals affected by them.

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