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## **Mixed Deep Learning for Analyzing Large-scale Substance Use Disorders Genetic Data**

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Artificial intelligence (AI) is a thriving research field with many successful applications in areas such as computer vision and protein structure prediction. Neural-network-based methods, such as deep learning, play a central role in modern AI technology. While neural-network-based methods also hold great promise for substance use disorders (SUD) genetic research, the high dimensionality of genetic data, the massive amounts of study samples, and the complex relationships between genetic variants and SUD bring tremendous challenges to use these methods in SUD genetic research. To address these challenges, we propose a new AI method based on mixed deep learning (MDL) for analyzing large-scale genetic datasets involving millions of variants and tens of thousands of samples. Unlike the classic neural networks, MDL models the overall genetic effects as random effects, which could substantially alleviate the overfitting issue and reduce the complexity of network structures. Random-effect neural networks and minimum norm quadratic unbiased estimation are implemented in MDL to model complex relationships (e.g., interactions) and accelerate the computation. Through simulations, we demonstrate the advantages of MDL over existing methods in terms of prediction accuracy and computational efficiency. We also apply MDL to the large-scale UK Biobank dataset, investigating high-dimensional risk prediction models for SUD.