Graph Neural Networks and Molecular Data Integration for Drug Repurposing in Neuropsychiatric Disorders

B. Patel[1], P. Lam[2], A. Khan[3], D. Panwala[4], E. Kim[5], N. Liang[6], P. Kavandal[7], S. Shoaib Hasnain[8], S. Aul[9], S. Yoele[10], T. Narynov[11], Z. Afroz[12]

[1]*Seattle University, Seattle, United States;* [2]*Sunset High School, Portland, United States;* [3]*University of Houston, Houston, United States;* [4]*Purdue University, West Lafayette, United States;* [5]*Centreville High School, Clifton, United States;* [6]*Pennsylvania State University, Centre County, United States;* [7]*Vista Del Lago High School, California, United States;* [8]*University of California, Berkeley, Berkeley, United States;* [9]*Columbia University, New York, United States;* [10]*West Ranch High School, California, United States;* [11]*High Bluff Academy, San Diego, United States;* [12]*Northgate High School, Walnut Creek, United States.*

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Objective

Our literature review aims to evaluate how graph neural networks (GNNs) integrated with molecular data enhance the prediction of drug repurposing candidates for neuropsychiatric disorders, with the aim of informing precision therapeutics.

Background

Neuropsychiatric disorders pose significant challenges to drug discovery due to their multifactorial etiology, diagnostic heterogeneity, and the high failure rates of clinical trials. Conventional drug development remains time-intensive and cost-prohibitive, averaging over 13 years and $1 billion per approved treatment. Drug repurposing offers a viable alternative, yet traditional approaches lack the capacity to identify nuanced gene–disease–drug relationships. Recent advances in GNNs offer a novel computational framework capable of modeling complex biological networks and uncovering latent therapeutic associations.

Methods

A comprehensive bibliometric analysis was conducted using the Web of Science Core Collection. An initial query using the terms "graph neural network," "drug repurposing," and "neuropsychiatric disorders" yielded 123 records. Articles published after 2020 were filtered, and the top 100 most cited publications were selected for in-depth review. Articles were systematically organized using Microsoft Excel to extract common methodologies, model architectures, molecular data types, and key findings.

Discussion

The convergence of GNN architectures and molecular data offers a transformative approach to drug repurposing, particularly for neuropsychiatric disorders where mechanistic heterogeneity and limited therapeutic options persist. While the current models show considerable promise, limitations related to interpretability, generalizability, and data sparsity remain. Enhancing model transparency through explainer modules and expanding high-quality, multimodal datasets will be critical to advancing this domain. Overall, GNN-based approaches represent a scalable and data-driven strategy for accelerating drug discovery in neuropsychiatric research.

Results

Several GNN models demonstrated significant promise in drug repurposing applications. Notably, the TxGNN model (Huang et al., 2024) achieved a 49.2% improvement in drug indication predictions through zero-shot learning and interpretable multi-hop pathways. Similarly, GDRNet (Doshi & Chepuri, 2022) effectively integrated gene expression and phenotype data to outperform other models in COVID-19 drug repurposing tasks. Across studies, the integration of molecular-level data—such as transcriptomic signatures, gene–disease associations, and pathway perturbations—was shown to enhance model performance and explainability. These findings underscore the potential of GNN frameworks to identify non-obvious therapeutic candidates in complex disorders.

Conclusion

Graph neural networks, when combined with rich molecular datasets, represent a significant advancement in the field of computational drug repurposing. Our analysis highlights their ability to improve predictive accuracy, generate interpretable insights, and uncover previously unrecognized therapeutic connections for neuropsychiatric disorders. As these tools continue to evolve, they hold the potential to streamline the development of safe, effective, and personalized treatments for complex neurological conditions.

Keyword 1: Graph Neural Networks
Keyword 2: Drug Repurposing
Keyword 3: Neuropsychiatric Disorders

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