CASE STUDY

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The Challenge

Schizophrenia drug discovery remains challenging because the relevant evidence is fragmented across heterogeneous biomedical resources and is difficult to analyse in a coherent, reusable form. Knowledge about disease mechanisms, drug actions, targets, pathways and phenotypes is distributed across databases with different schemas and standards, while additional mechanistic and clinical evidence remains embedded in unstructured literature. For complex psychiatric disorders, this fragmentation limits systematic integration, weakens cross-resource reasoning, and constrains robust hypothesis generation for drug repurposing.

A further challenge is that, although deep learning and other computational drug-prediction models can rank candidate drugs and targets, many of these approaches remain insufficiently interpretable for expert-facing biomedical use. In practice, schizophrenia repurposing research requires not only candidate prediction, but also biologically meaningful justification that researchers can inspect, assess and relate back to known evidence.

This creates the need for a schizophrenia-focused, structured and extensible resource that integrates curated biomedical knowledge, supports computational ranking, and enables expert-guided interpretation of why a candidate may be relevant.

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Innovation

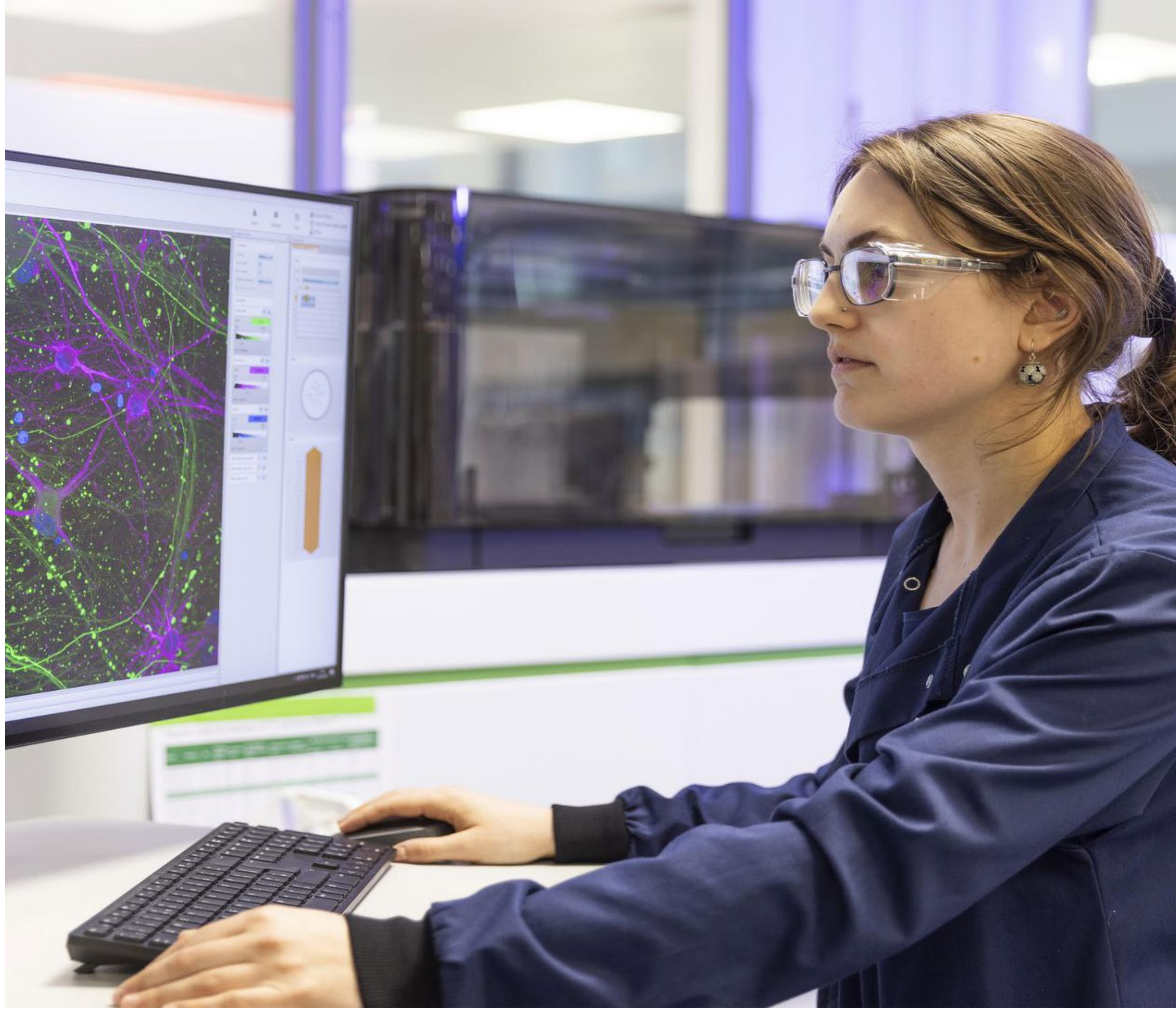
A modular research pipeline was developed to construct a schizophrenia-centred knowledge graph from curated biomedical sources. The work included literature review, schema design, source mapping, raw knowledge extraction, identifier harmonisation, enrichment through external biomedical services, and graph construction in Neo4j. The schema was developed as a multi-layered mental-health schema, designed to represent schizophrenia across different levels of biomedical knowledge.
To support candidate generation, graph embeddings were trained using the large biomedical knowledge graphs and fine-tuned on the schizophrenia specific knowledge graph using transfer learning. This crucial step allowed our system to understand information within the broader biomedical structure, beyond the immediate schizophrenia neighbourhood, enabling better drug repurposing hypothesis generation.
To support interpretation, a metapath-based reasoning approach was developed to assess candidate drugs through biologically meaningful paths. These components were made accessible through a user-facing interface supporting knowledge-graph question answering, candidate ranking and evidence-based candidate analysis.
The project was delivered through a highly configurable architecture so that the graph, enrichment services and predictive components can be maintained and extended in future work or adapted to other disorders.

Result

The results of the project are demonstrated via its technical outputs: a schizophrenia-centred knowledge graph populated from curated open data sources, an embedding-based drug candidate ranker, and a metapath-based reasoning approach for candidate assessment. Collectively, these outputs moved the work from concept to a functional prototype for schizophrenia-focused drug repurposing.
A key lesson from the project was the value of combining predictive ranking with interpretable graph-based reasoning. As an illustrative case, the ranker prioritised minocycline as a high-confidence candidate for schizophrenia. Minocycline is an established tetracycline drug used for bacterial infections and some acne indications, but it is not formally approved for schizophrenia. The metapath-based reasoner then provided a biological explanation for this ranking by identifying plausible links through genes, pathways and biological processes that overlap with mechanisms associated with existing schizophrenia treatments. This is important because recent drug-repurposing research increasingly emphasises that explainable, path-based reasoning is needed to complement predictive models whose outputs may otherwise remain difficult for experts to interpret and assess.
This example was also informative scientifically. Existing literature has repeatedly investigated minocycline as an adjunctive candidate in schizophrenia, particularly for negative symptoms, but findings remain mixed and overall inconclusive. The main lesson, therefore, was not that the model confirmed minocycline as a treatment, but that it could recover a literature-supported candidate and provide an interpretable rationale for why that candidate may warrant further expert investigation.

Impact

The project's impact lies in showing a credible route from academic AI research to a more usable drug-repurposing workflow for severe mental illness. Its immediate value is the creation of a schizophrenia-focused, structured resource that brings together curated biomedical knowledge, supports candidate ranking, and adds interpretable biological context to those rankings. This matters because knowledge-graph approaches are increasingly recognised as effective for drug repurposing, while explainability is now seen as essential for trust, transparency and expert assessment of AI-generated candidates.
The wider potential is sectoral. Rather than producing only another prediction model, the project demonstrates a reusable methodology for integrating heterogeneous biomedical data, enriching disorder-specific knowledge graphs, ranking candidate drugs, and tracing mechanistic support through biologically meaningful paths. In practical terms, this could help research teams move faster from fragmented evidence to prioritised, reviewable hypotheses, improving how candidate treatments are identified and assessed in translational research settings. Because the framework is modular and disease-focused, it is also adaptable beyond schizophrenia to other complex disorders where evidence is distributed across many resources and expert justification is required before further validation. In that sense, the work has potential to support research centres, innovation programmes and industry-facing discovery teams not only by generating candidates, but by making those candidates more interpretable, auditable and actionable for downstream scientific decision-making.



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"Working with Dr Papadakis has allowed us to access a novel tool to categorise relationships between drugs, targets and patient outcomes in the complex aetiology of Schizophrenia. This AI-driven knowledge graph is, to our knowledge, the first of its kind and has the potential to enable researchers to identify novel therapeutic opportunities. It has been a pleasure to work with Dr Papadakis and hope to remain engaged after the RiR project to assist with translation and community engagement."

Emmanuel Papadakis

"Working with Medicines Discovery Catapult helped me translate AI research in mental health into a practical framework for schizophrenia drug repurposing."

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