Using PathFX to Find Novel Drug Pathways to Treat Schizophrenia, Bipolar Disorder, and Major Depressive Disorder/Unipolar Depression

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Abstract

Schizophrenia (SCZ), Bipolar Disorder (BPD), Major Depressive Disorder (MDD)/Unipolar Disorder (UD) are commonly comorbid diseases, though they are often treated individually. Combination treatments increase the chance of adverse reactions, begetting the need for single-drugs or lower variation of drugs to treat comorbid conditions. Many, including ourselves have used protein-protein interaction (PPI) network models to model drug effects. We used our PPI method, PathFX, to identify drugs with associations to multiple psychiatric diseases and identified shared proteins in these predictions. We discovered several shared proteins GNB1, POMC, SST5, APP, OXT, GRM5, HCRT, NPY, CHRM3, and SST to be associated with these phenotypes. By assessing shared pathways we predicted several single-drug options for comorbid psychiatric treatments, but we require further assessment to validate these predictions as treatments.

Method

1. Generate PathFX networks for all approved drugs
2. Assessment of PathFX predictions for four psychiatric diseases
3. Analysis of most common pathway genes across and within diseases
4. Literature review of PathFX predictions

Results

Figure II: Bar graph counting the times a protein occurs in a drug pathway for BPD, UD-MDD, or SCZ. 634 unique proteins were found to associate with at least one drug pathway.

Conclusion

- Network analysis via PathFX has revealed common genes and proteins for SCZ, BPD, and MDD/UD.
- Novel drugs to treat these disorders has been found (e.g., dihydromorphine).
- Further experimental tests and analyses are required to understand these pathways and how they could then be applied to treating patients.

References


Acknowledgements

Special thanks to Dr. Jennifer L. Wilson, the Lab for Understanding Network Effects at UCLA, the UCLA Department of Bioengineering, and the UCLA Bruins-In-Genomics (B.I.G.) Summer Program. This project was funded by NIH: NIDCR Grant Number R25DE030117.