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Computational Analysis of Network Model Based Relationship of Mental Disorder with Depression

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Abstract: In this study, we present the network relationship of anxiety, eating and mood disorder with depression. Different computational network models have been demonstrated using different ongoing technologies. One of the most common mental illnesses can be classified as anxiety disorders. These are observable psychological conditions or a category of mental illnesses believed to be caused either by genetic weakness or by causes of environmental sensitivity. A wide range of psychological chronic conditions is often correlated with eating disorders (ED). However, the increasing role of lipid metabolism in ED pathogenesis has been highlighted by recent research studies. Depression (DE) acknowledgement is traced back to the ancient Greeks, who called it melancholia. The word depression has originated with the Greeks who used it to identify a specific condition, a God-given spiritual state, or a response involving rage or excitement, in different ways. Throughout drug research and development, finding innovative mechanisms is a massive challenge. In this field, structure-based design is a basic methodology and has become an essential part of developing drugs. The detailed three-dimensional structure of the protein is shown for a significant number of drug targets. While simulation docking and similar biotechnology have progressed in recent times, a suitable set of docking simulations for simulation performance is difficult to identify.

Keywords: Mental disorder; Protein-protein interaction; Protein-drug interaction; Anxiety disorder; Eating disorder; Depression; Mood disorder.
Abbreviation: NCBI = National Center of Biotechnology Information; AD = Anxiety Disorder; DE = Depression; ED= Eating Disorder; MD = Mood Disorder; PPI = Protein-protein Interaction; PDI = Protein Drug Interaction; PCI = Protein Chemical Interaction.

1. Introduction

There are a wide number of problems with mental disorders, with different symptoms. We are described, however, by some mixture of irregular feelings, emotions, actions, and

interactions with others. Most of these diseases could be treated successfully. Anxiety disorders (AD) are a category of mental disorders with severe anxiety and fear feelings. Anxiety is a concern for events in the future, and fear is a reaction to present events. These physical effects can cause physical symptoms, such as rapid heart rate and shakiness [1, 2]. DE is a common disease of the mind. About 264 million people of all ages worldwide are suffering from DE [3]. DE is one of the world's leading causes of illness and a significant contributor to the worldwide disease burden. DE affects more women than men [3]. For moderate and severe DE, effective psychological and pharmacological interventions occur.

ED is a major health problem in Western countries and particularly among young people [4,5]. ED is very dynamic and lacks a pathophysiological description and is medically accepted by the specific clinical guidelines of the Fifth Edition of the Mental Disorders Diagnosis and Statistical Manual, published by the American Psychiatric Association [6]. Anxiety or mood disorders can be associated with ED; migraines; as well as physiological problems such as cardiac abnormalities, hormonal imbalances and a wide array of gastrointestinal (GI) symptoms [7]. Mood disorders (MD) are a set of psychiatric diseases that can impact one's emotional responses, energy and motivation at the same time [8]. MD can sometimes be linked to effective disorders. Psychiatrists began to recognize signs of mood disorders in infants, adolescents and adults during the 1980s [9].

Finding the characteristics of infection is important to understand the components of physiological and obsessive sickness procedures. It takes time to perform tests to confirm those characteristics linked to infection. Numerous analytical methods and tools have been developed to coordinate disease attributes in order to increase proficiency. Complex interactions among the different constituents of the cell, such as protein, DNA, RNA, and other small atoms, are effective in making Biological capabilities. The research work on screen has connected a framework for bioinformatics to create a model of performance and cooperation scheme by taking high-performance genomic and PPI data for AD, DE, ED and MD.

2. Materials and Methods

Bioinformatics has been applied in a limited number of previous research works involving the analysis of liable genes, the development of PPI networks, regulatory networks, and the possible interaction of drug proteins for specific 4 disorders. In this analysis, several steps are taken to achieve a better outcome. From information accumulation to the protein-chemical interaction network, some individual developments are made here. Figure 1 indicates the research methodology's graphical representation step by step. That phase is also listed below in the following subsections under 2.1 to 2.8.

2.1. Data collection.

Bioinformatics software and utilities have very few reliable databases. AD, DE, ED and MD study results are gathered from the NCBI Gene database. The gene NCBI database is available for free and can be downloaded. Upon extracting responsible genes, it was reprocessed and screened for any further processing.

2.2. Preprocessing.

In the past, each of the features linked to AD, DE, ED and MD are collected. In this stage, just genes related to Homo sapiens are collected. They are primarily categorized and all

other genes that are obtained are processed and only responsible genes that are responsible for human diseases are kept for the next process.

2.3. Gene mining.

The data mining technique is mainly used to produce appropriate data. Gene mining is among the most important areas of this research as any type of error can reject a substantial gene that occurs in the wrong outcome. Only the genes are extracted from the records of the sorted linkage genes. Afterward, genes are recognized and sorted in relation to each other. Using the intersection data mining method, the listed candidate genes linked to AD, DE, ED and MD were mined.

2.4. Generic PPI.

In bioinformatics, research into protein-protein interaction or PPI network plays a significant role. The PPI network often facilitates the knowledge of human disease genetic signaling pathways and the development of a new framework of disease pathways. Cytoscape is a very well-known and trusted bioinformatics research tool used to create PPI networks [10]. Targeted 4 diseases are developed from interconnected common genes of PPI networks and common pathways using Cytoscape in this process.

2.5. Gene regulatory network.

Gene regulation is a scientific term for a variety of concurrent processes, a well-known and well-understood one of which is encoding and translation, which controls the amount of gene expression and ultimately results in a specific number of the target protein. Regulators are most generally proteins, called transcription factors, but the general regulation often includes tiny molecules, such as RNAs and metabolites. Depending on the degree of abstract concept and accessibility of scientific information, there are different levels of gene network modeling [12].

2.6. Protein drug interaction.

Work on the interaction of protein drugs is of crucial importance in order to understand the fundamental characteristics of molecule affinity [13]. One way of resolving this, discrepancy is done by using computational methods to determine protein targets for a given drug molecule or to interact with drugs for specific protein targets [14]. Interaction with protein drugs is developed for all targeted 4 diseases ' interconnected, liable, prevalent genes.

2.7. Protein chemical interaction.

The portion of the biochemical environment that has been identified is that and a significant percentage of established protein-chemical relationships are becoming accessible for research studies. Protein – Chemical interaction data are spread across a wide variety of datasets and literature, making it difficult to evaluate the known relationships of any significant chemicals [15]. Co-expression networks are transcript-transcript interaction networks, usually calculated as undirected maps, where genes are connected when a large co-expression connection occurs between them.

2.8. Co-expression & physical interaction.

Co-expression networks could be used to integrate unidentified function genes with biological processes, to coordinate genes for rival disease, or to track programmed gene expression regulations. Co-expression networks are interpreted by calculating co-expression values on a pair-related score of gene interaction and defining a significance level from information on gene expression. Discussions on standardization methods, co-expression similarity, meaning, and significance are still alive and ongoing. Trends in this sector included the combination of co-expression evaluation with separate omics methodologies, such as metabolomics, to determine the scheduled behavior between gene expression and metabolites, and to evaluate metabolite-regulated genetic networks among different methodologies [16].

3. Results and Discussion

3.1. Gene collection.

The liable genes for specific diseases retrieved from the NCBI database. The outcome shows respectively 37, 1101, 32 and 45 liable genes for AD, DE, ED and MD. There are 34 for AD, 537 for DE, 30 for ED and 42 for MD since processioning and sorting the associated genes for Homo sapiens. The genes are sorted in ascending order by their weight. The numerical values of identified liable genes are shown in Table 1.

3.2. Gene mining, linkage & common gene finding.

It identifies the linkages between AD and DE, AD and ED, AD and MD, DE and ED, DE and MD, ED and MD, AD and DE and ED, AD and DE and MD, AD and ED and MD, DE and ED and MD, AD and DE and ED and MD. The numbers of common liable genes are discovered between 4 selected diseases after gene linkage. The 4 weighted genes are kept to avoid complicated results [20]. The 4 weighted genes are SLC6A4, BDNF, COMT, DRD2. Figure 2 indicates the Venn analysis of the number of gene and the common gene ratio. The genes are extracted from the trusted database at the beginning of this research. After that, the data set was applied to the mining algorithm. In addition, there has been a rigorous analysis of the intersection of two, three and four diseases. We placed 34 no of gene for AD, 537 no gene for DE, 30 no gene for ED and 42 no gene for MD in the Venn diagram study. After Venn analysis, we get 16+6+4+4=30 no of common gene between AD & DE; 6+4=10 no of common gene between AD& ED; 4+4=8 no of common gene between AD& MD; 6+9+4+1=20 no of common gene between DE & ED; 4+1+4+16=25 no of common gene between DE & MD; 4+1=5 no of common gene between ED & MD; 6+4=10 no of common gene between AD & DE &ED; 4+4=8 no of common gene between AD & DE & MD; 4 no of common gene between AD & ED & MD; 1+4=5 no of common gene between DE & ED & MD; For AD & DE & ED & MD we get 4 no of common gene between them. Table 2 and Figure 2 reflect with each other after the investigation, so our study has been verified.

3.3. Generic PPI.

ToppGene is a comprehensive internet tool designed to enable committee researchers to perform routine and complex meta-examinations of data on gene expression using a natural web interface [17]. The PPI network is the link between genes and hub protein that are directly linked to others that are indirectly linked to each other. XGMML files are generated using the

ToppGene web-based platform using the network-based k-Step Markov prioritization approach for the network diagram. By using XGMML file in Cytoscape, we develop the network and represent it in Figure 3 for selected 4 genes.

3.4. Enrichment Analysis.

In this paper, we propose a flexible and powerful framework for mining regional imaging genetic associations via voxel wise enrichment analysis, which embraces the collective effect of weak voxel-level signals and integrates brain anatomical annotation information [11]. WebGestalt (WEB-based Gene SeT AnaLysis Toolkit) is a functional enrichment analysis web tool [18]. By using WeGestalt tool, we select Network Topology-based analysis (NTA) as Method of Interset and also used network-based PPI BIOGRID as Functional Database for Homo sapiens for responsible 4 genes (SLC6A4, BDNF, COMT, DRD2). Figure 4 represents the enriched GO terms Graphs.

3.5. Enrichment analysis.

We have 4 genes responsible for building to establish genetic activity and pathways (SLC6A4, BDNF, COMT, DRD2). GeneMANIA is one of the most commonly available online tools in the linked gene network to predict gene function [19]. Figure 5 and Figure 6, respectively, show the co-expression and physical interaction using the GeneMANIA tool. STRING database provides a network to show the direct links between the 4 genes responsible for the 4 diseases targeted. STRING is a web-based method for the interaction of genes with other molecular biology's [20]. The direct interaction between 4 genes is shown in Figure 12.

3.6. Gene regulatory network.

Gene regulatory networks vary from stronger-known communication networks between proteins and proteins, as two-party and lateral gene regulatory networks. To describe the gene regulatory network, we used web-based NetworkAnalyst tools. There are three types of gene regulatory network: Gene-miRNA interaction, TF-gene interaction, TF-miRNA co-regulatory network [21-22]. Gene-miRNA interaction, TF-gene interaction, TF-miRNA co-regulatory network are shown in Figure 7, Figure 8, and Figure 9, respectively.

3.7. Protein drug interaction.

Structural and mechanical assessment of the protein target during drug development is an important issue, preferably coupled with a multi-level understanding of how ligand binding modulates conformation and biological function [23]. By interacting with other proteins and ligands, proteins perform their roles in the cell. The complete set of drugs that can be used for the above selected disease is shown in Figure 10 PDI. The NetworkAnalyst tool generated PDI network and developed by Cytoscape.

3.8. Protein chemical interaction.

Biochemical networks are now helping to initiate a number of important human behavior research and disease prevention [24]. Interactions between proteins and small molecules are an integral part of biological processes in living organisms [25]. Figure 11 shows a protein-chemical interaction. The PCI is generated using the NetworkAnalyst tool. Finally, it

can say that the analysis of gene regulatory netwrok or drug-protien interaction netwrok of this work like the articles [26, 27] will be most helpful for design future computational drug model [28, 29].

Figure 1. Flowchart of the Methodology offered.

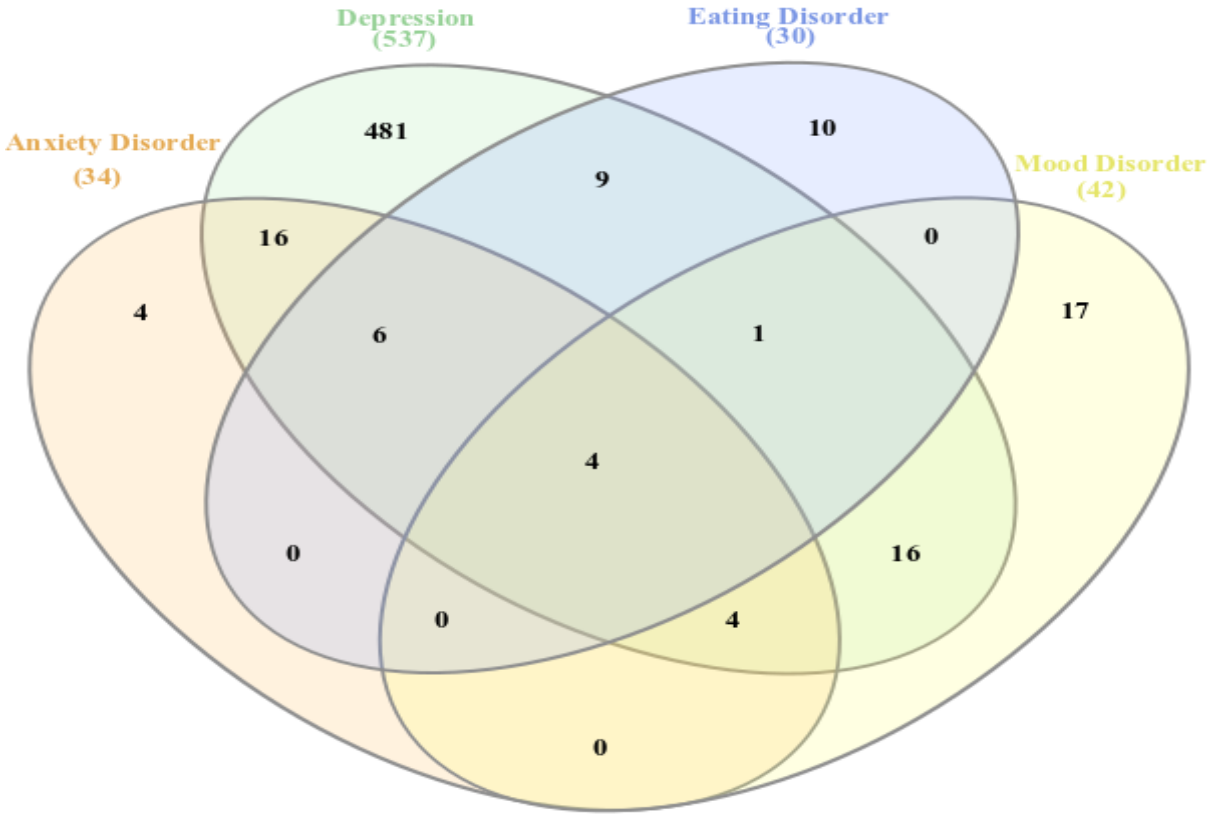

Figure 2. Venn diagram for selected 4 diseases.

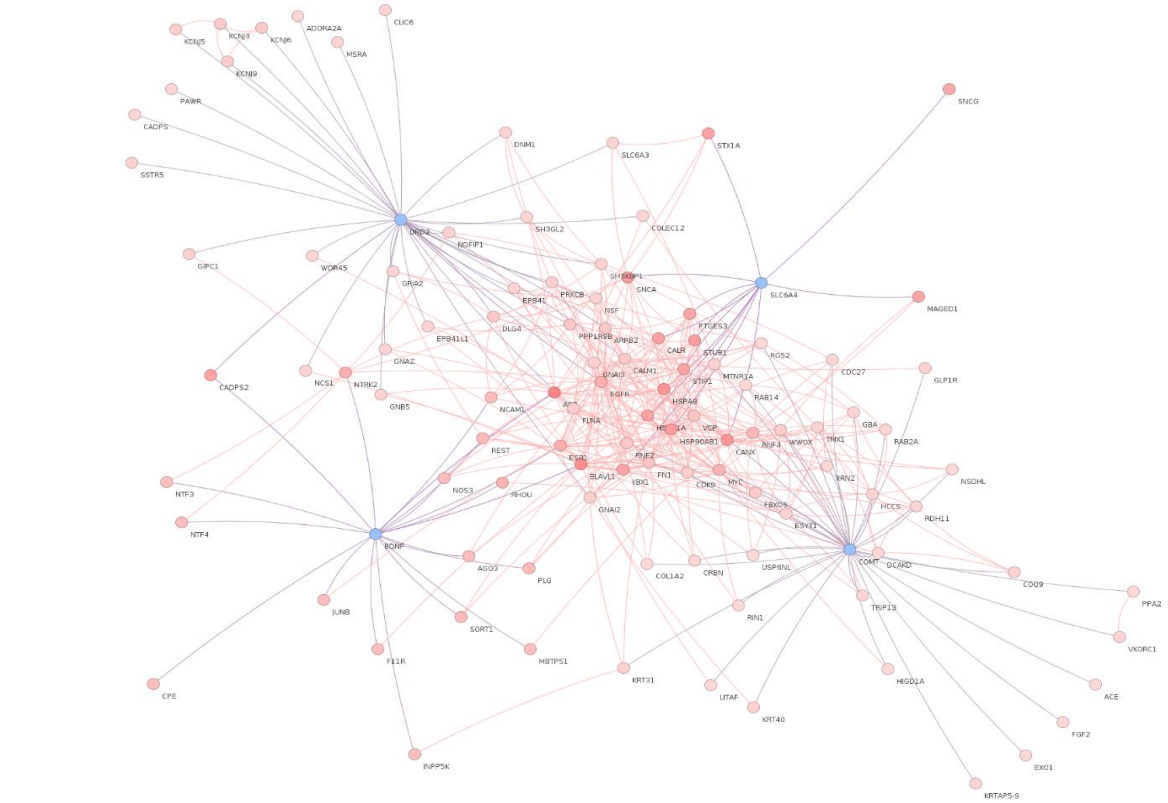

Figure 3. A network of 4 common responsible genes for PPI. There are 108 nodes and 440 edges to be built in the network. Nodes are proteins, and the edges establish a relationship between proteins.

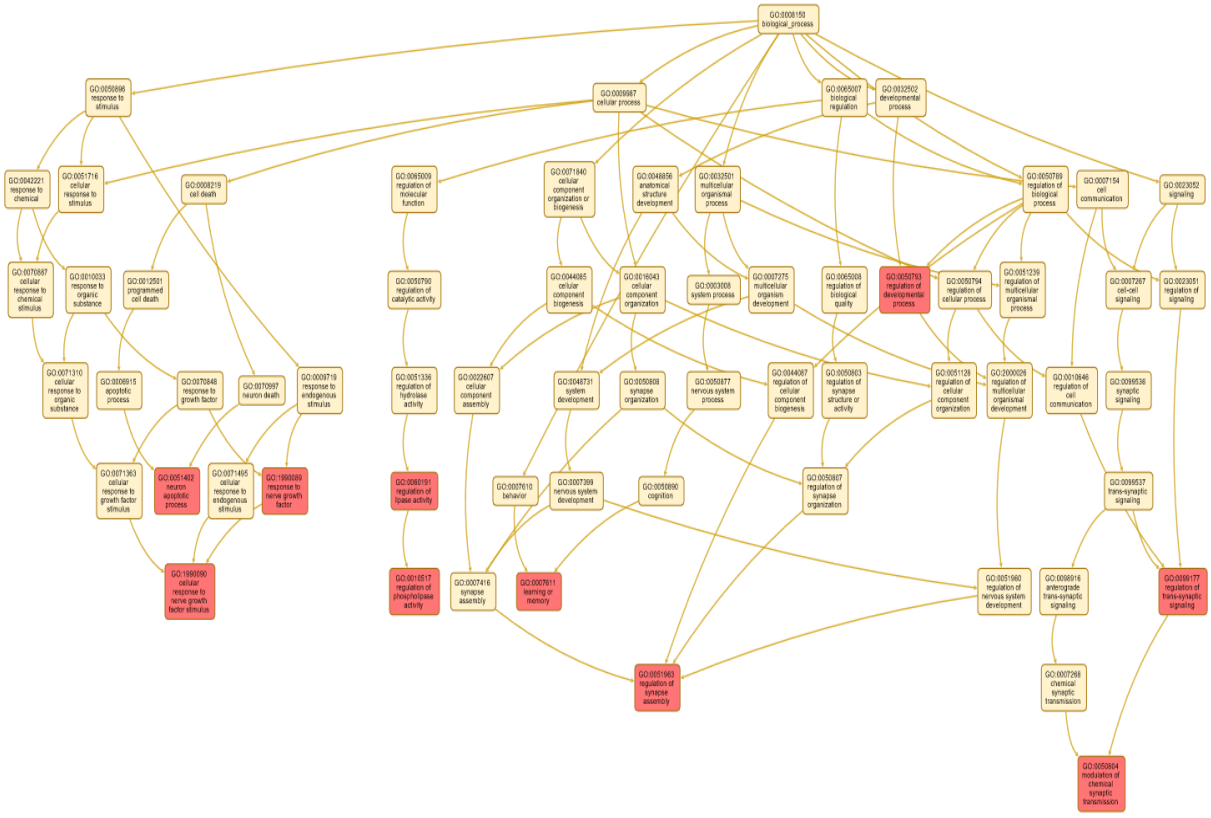

Figure 4. Enriched GO terms Graphs.

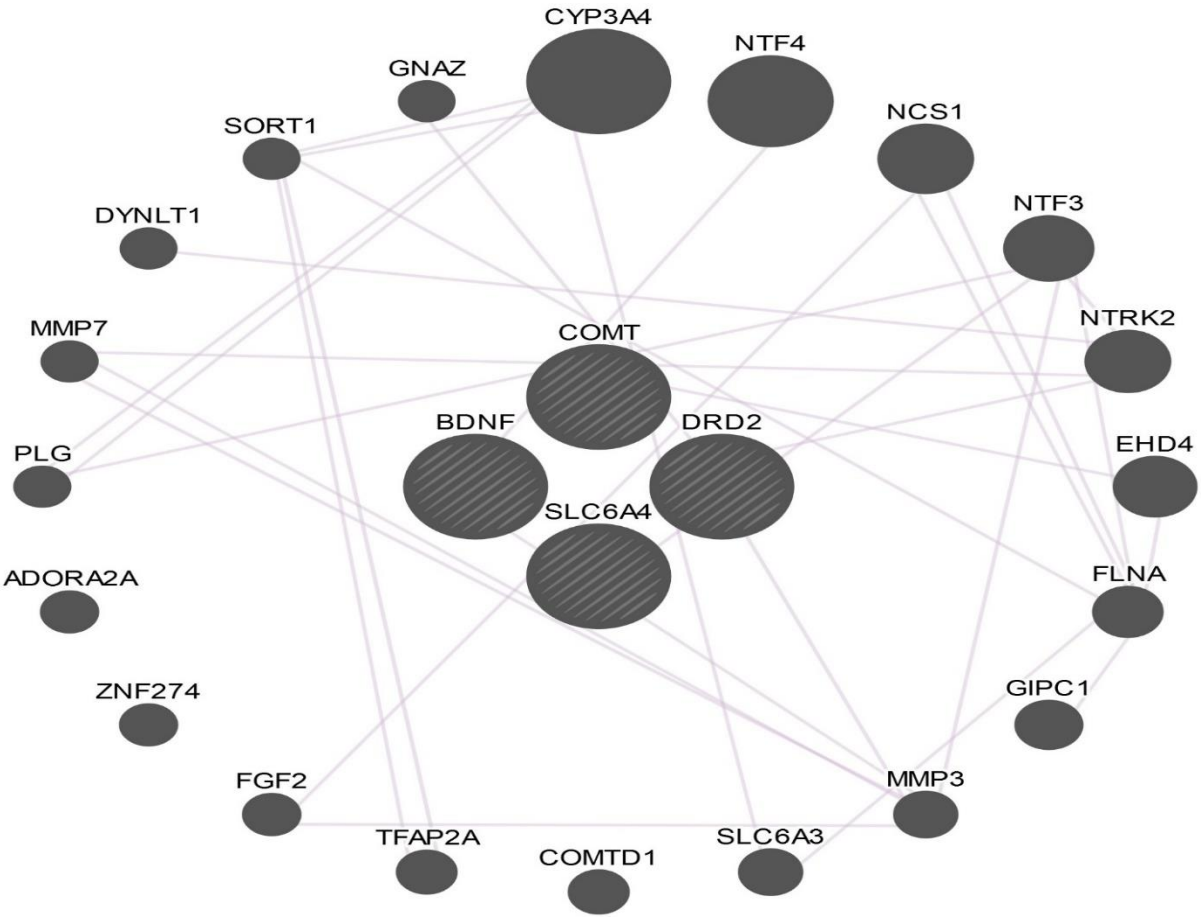

Figure 5. Co-expression between SLC6A4, BDNF, COMT, DRD2.

Figure 6. Physical Interaction between SLC6A4, BDNF, COMT, DRD2.

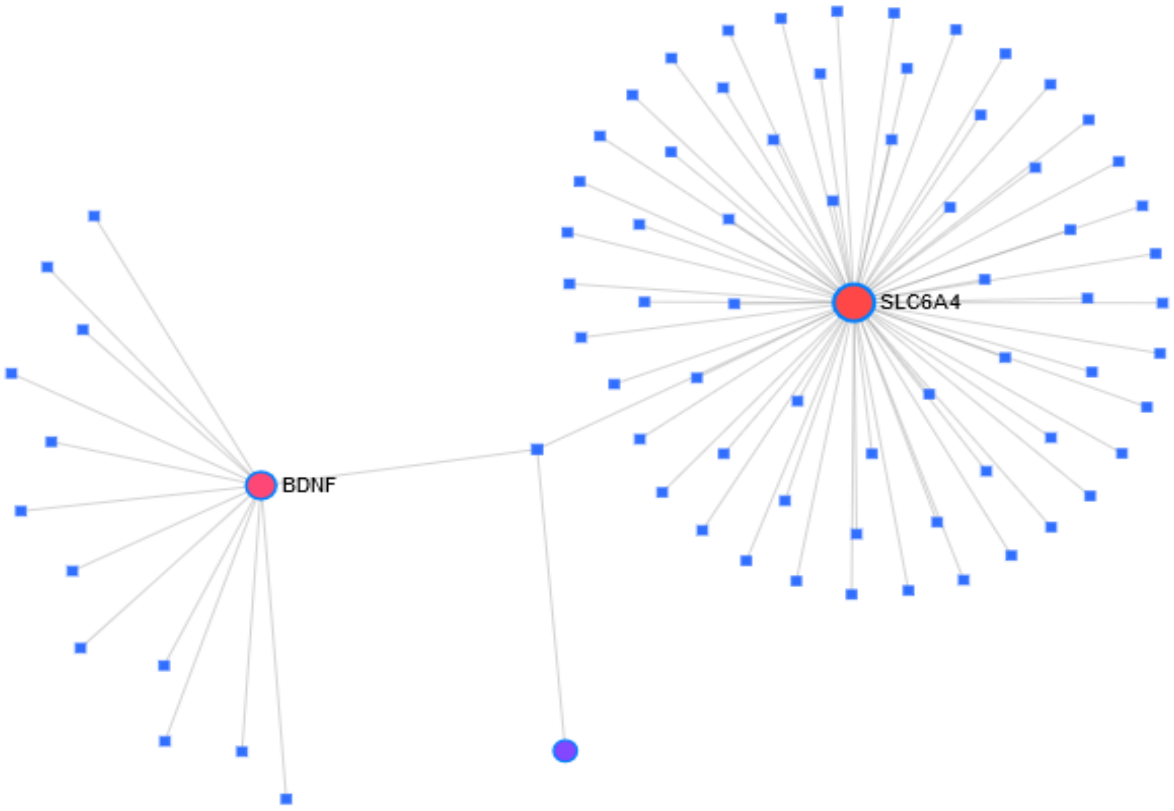

Figure 7. Gene -miRNA Interaction for selected 4 genes. This gene-miRNA interaction generates interactions with a total of 78 links between 79 genes.

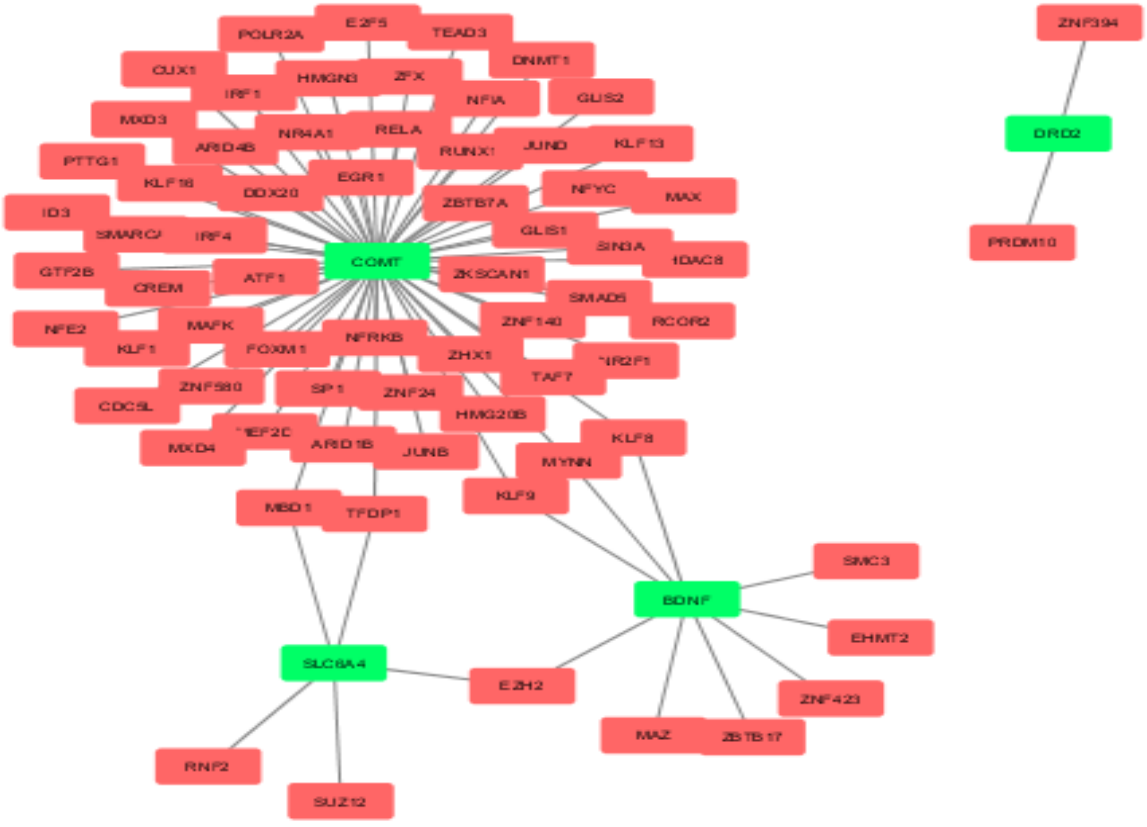

Figure 8. TF-gene Interaction for selected 4 genes. This TF-gene Interaction creates relationships between 73 proteins with a total of 75 connections.

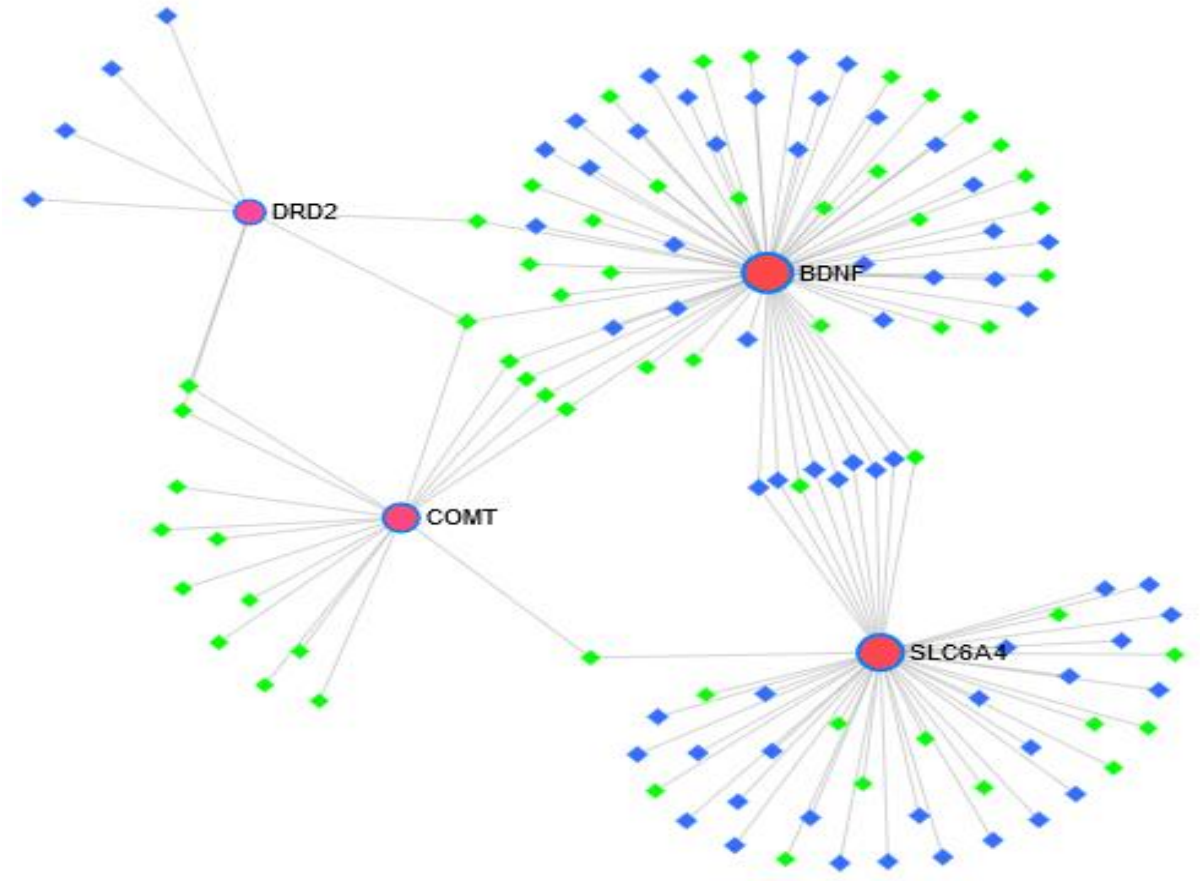

Figure 9. TF-miRNA co-regulatory network for selected 4 genes. This TF-miRNA coregulatory network creates relationships between 3678 proteins with a total of 4530 connections.

Table 1. The number of responsibility genes for selected diseases obtained from the NCBI database.

Diseases Name	Total no of gene	Total no of Homo sapiens
Anxiety Disorder (AD)	37	34
Depression (DE)	1101	537
Eating Disorder (ED)	32	30
Mood Disorder (MD)	45	42

Table 2. The no of common gene between selected 4 diseases during the intersection process.

Disease	Total no. of gene	Common gene
AD & DE	571	30
AD & ED	64	10
AD & MD	76	8
DE & ED	567	20
DE & MD	579	25
ED & MD	72	5
AD & DE &ED	601	10
AD & DE & MD	613	8
AD & ED & MD	106	4
DE & ED & MD	609	5
AD & DE & ED & MD	643	4

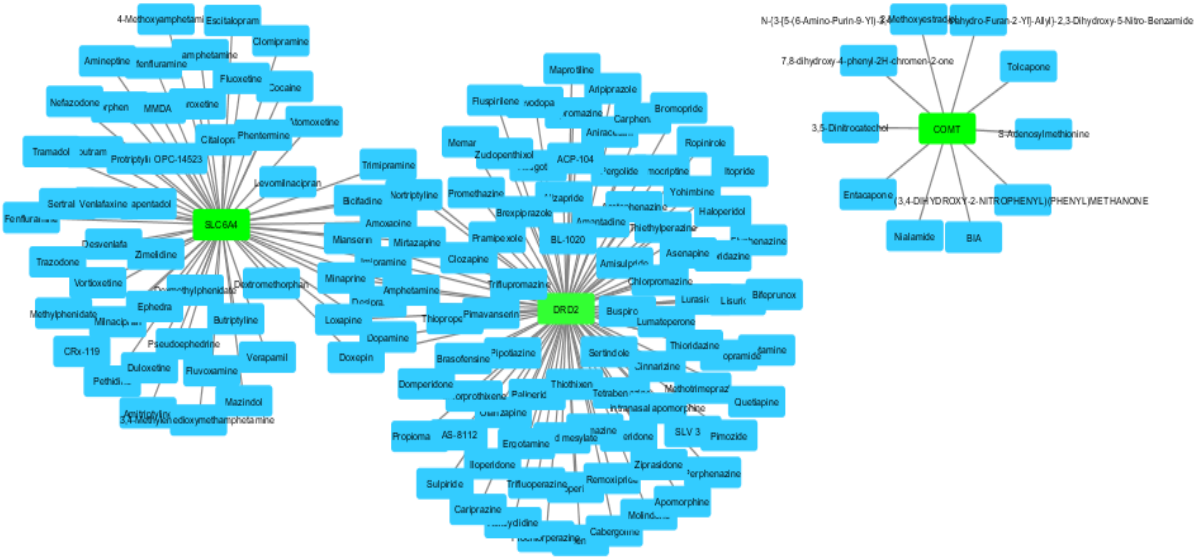

Figure 10. Protein-drug interaction for selected 4 genes. This PDI creates relationships between 147 proteins with a total of 157 connections.

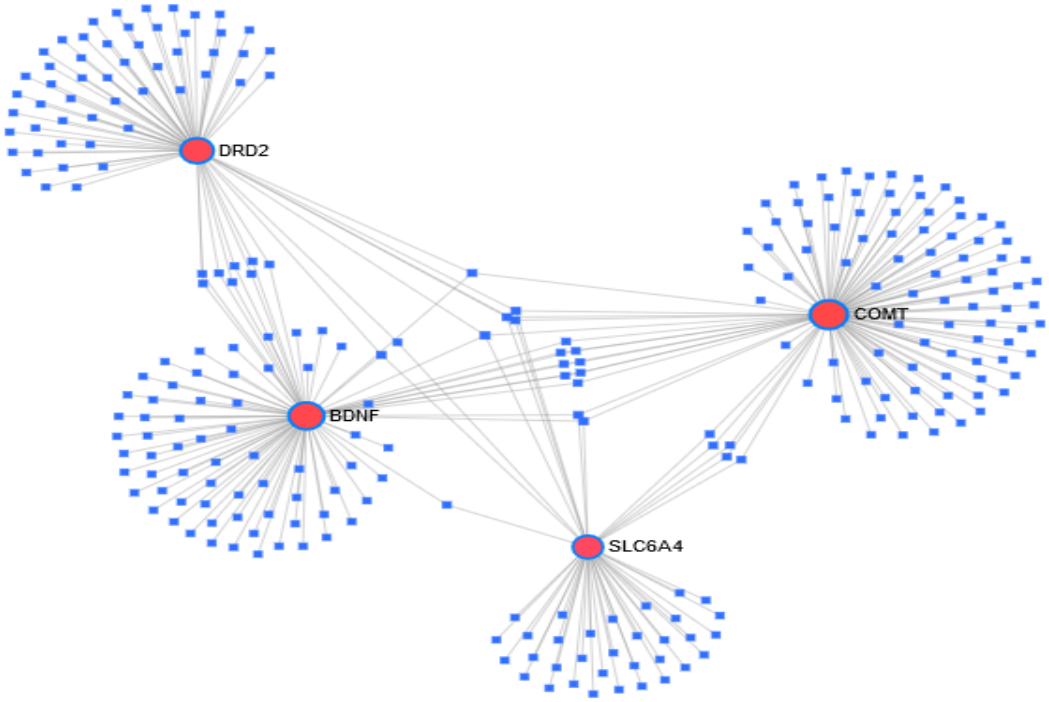

Figure 11. Protein-chemical interaction for selected 4 genes. This PDI creates relationships between 273 proteins with a total of 309 connections.

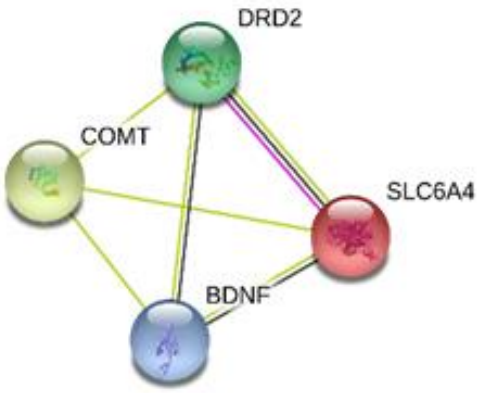

Figure 12. Connecting 4 genes (SLC6A4, BDNF, COMT, DRD2) using the STRING database. The network demonstrates the common genes inter relationship.

4. Conclusions

We have presented an overview of four disease: AD, DE, ED and MD. Cross-connection of mental illeness demonstrates the relationship between them at the gene level. In the so-called "Post-genomic Era," one of the most interesting and important problems is the interpretation of protein networks. Most of our understanding of drugs, drug pathways and drug receptors could fit into a few encyclopedic books and a few hundred schematic figures until the 1980s. Moreover, this is no longer the case with the recent explosion in biological and chemical information. The creation of medicine-binding databases plays a crucial role in understanding the relationship between protein and drug interaction [30]. Enhancements to the bioinformatics platform have demonstrated new field of study and created uncompromising tasks simpler than before. From these study results of the related susceptible genes between linked diseases, it will be useful to investigate both the diseases and the accurate design of drugs. This research also helps to understand the PPI, the regulatory gene network, the protein-drug interaction, and the protein-chemical interaction. The purpose of this study is to understand the network of genes for metabolism and to improve drug design.

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Conflicts of Interest

The authors declare no conflict of interest.

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