Database of gene polymorphisms in different psychiatric disorders

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MAY-2013

Submitted in partial fulfillment of the degree of Bachelor of Technology

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CERTIFICATE

This is to certify that the work titled "**GENE POLYMORPHISMS IN DIFFERENT PSYCHIATRIC DISORDERS DATABASE**", submitted by **Nidhi Aggarwal (091557)** in partial fulfillment for the award of degree of Bachelor of Technology in Biotechnology of Jaypee University of Information Technology, Waknaghat, has been carried out under my supervision.

This work has not been submitted partially or fully to any other University or Institute for the award of this or any other degree or diploma.

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ACKNOWLEDGEMENT

I gratefully acknowledge the Management and Administration of Jaypee University of Information Technology for providing me the opportunity and hence the environment to initiate and complete my project.

I would like to express my gratitude to **Prof. Dr. R.S. Chauhan,** Head of the Department, Biotechnology and Bioinformatics JUIT, Waknaghat for guiding, encouraging and inspiring by giving me valuable thoughts to carry out the project.

I would also like to thank my project guide, **Dr. Jayashree Ramana**, Senior Lecturer, Dept. of Biotechnology and Bioinformatics for her expert guidance, encouragement and valuable suggestions at every step. She has been an inspiration as I hurdled through all the obstacles in the completion of this research work.

Apart from these, countless people and several events have made a contribution to this project which is indescribable. I again express my gratitude to them. I am indebted to all those who provided reviews and suggestions for improving the results and topics covered in the project, and extend my apologies to any one whom I have failed to recognize in this effort of ours.

I would like to acknowledge JUIT for providing me the facility to host the PsychDB database.

Nidhi Aggarwal

Date: 25/05/2013 Nidhi Aggarwal (091557)

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ABSTRACT

Psychiatric disorders are one of the common devastating disorders affecting 26% of the people over age of 18 throughout the world. Currently there is no treatment available for any psychiatric disorder. Also the etiology and diagnosis are subjects of ongoing debate. Common strategies for the treatment of these disorders involve psychotherapy, medication etc. But they just help in alleviating the symptoms to some extent. A major problem in finding the cure of the disease is little understanding about the molecular aspects of every disorder. So, researchers have identified genes involved in development and pathogenesis of these disorders through a number of techniques. However, all this information is scattered in literature and is therefore not amenable to integrated analysis. In past few years, many related databases have been developed but they have various limitations. In order to reduce this gap, this project describes a comprehensive repository, PsychDB, compiling data related to psychiatric disorders. PsychDB, Psychiatric Disorder Mutation Database is a manually curated database of 7 psychiatric disorders containing 445 genes and more than 1300 mutations in total contributing to the etiology and pathogenesis of these disorders. Genes are categorized under different psychiatric disorders and mutations are shown for each gene related to a particular disorder. Users can query the database using different options. Users can search for a particular disorder or a particular gene for the relevant information. In addition, user can search for common genes in any two disorders and can look for the mutations in each disorder. The database can be freely accessed via a user friendly web interface at http://juit.ac.in/attachments/PsychDB

It is hoped that this database would serve as a useful resource to the academic and research community.

CHAPTER-1

INTRODUCTION

1.1 Psychiatric Disorders

Psychiatric disorder (or mental disorder) is a psychological anomaly which is commonly associated with disability or distress [1]. They involve disturbance of thought, experience and emotion which are serious enough to cause functional impairment in patients. As a result, the patients suffer difficulty in sustaining their interpersonal relationships and carry on their jobs. Also it may lead to self destructive behavior and even suicide [2]. They are associated with particular region/ function of brain or nervous system.

1.1.1 Classification

Classification of psychiatric disorders is an issue of ongoing debate. Currently there are two widely established systems to classify psychiatric disorders. One is the **Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)** by the American Psychiatric Association (APA) since 1952. Other is **ICD-10 Chapter V: Mental and Behavioral Disorders,** since 1949 part of the International Classification of Diseases by the WHO. Both the classifications list categories of disorder and provide standardized criteria for diagnosis [1]. The DSM-IV describes approximately 250 different psychological disorders [3].

There are different categories of psychiatric disorder – anxiety disorder, mood disorder, developmental disorder, cognitive disorder, personality disorder, eating disorder, sleep disorder etc [1].

According to National Institute of Mental Health (NIMH), ~26% of people over age of 18 suffer from some type of psychological disorder [3].

1.1.2 Causes

There are various causes of psychiatric disorders. In many cases, there is no single cause for the disease. There are various theories and models to explain particular disorders. A common assumption has been taken that disorders may have resulted from genetic and developmental vulnerabilities, exposed by stress in life, although there are again various theories on what causes differences between individuals.

Some studies indicate that variation in genes play a significant role in the development of psychiatric disorders. Also the environmental events at the time of pregnancy and birth have been seen. It has been observed that social influences are important in development of psychiatric disorders. This includes abuse, social stress, bullying, neglect or any other negative life experiences. Apart from above mentioned factors, abnormal functioning of neurotransmitter systems and difference in the size or activity of certain brain regions have been observed in many of cases [1].

The specific risks and pathways involved in any particular disorder are less clear. So, a lot of focus is placed on revealing the genetic aspects of psychiatric disorders so as to find a permanent cure for such disorders [1].

1.2 Gene Polymorphisms

Polymorphisms occur when two or more clearly different phenotypes exist in the same population of a species [4]. A Single Nucleotide Polymorphism (SNP) is a change of a single nucleotide (A, T, C, G) in the genome. The genomic distribution of SNPs is not homogenous.

SNPs can occur in the coding sequence of genes, non coding regions of genes or in the intergenic sequence. SNPs in the coding region are of 2 types – synonymous and non synonymous. Synonymous SNPs do not change the protein sequence while non synonymous change the protein sequence.

Non synonymous SNPs are further of two types: Missense and non sense

Study of SNPs is very important in biomedical research. Variation in DNA sequences can affect how an individual develop diseases and respond to various environmental factors. SNPs have greatly been used in genome-wide association studies (GWAS). Study of SNPs also helps in understanding how a drug acts in different individuals with different genetic variants [5-6]. Generally SNPs do not directly cause a disease but alter the risk of developing a disease. By analyzing the genotypes of a collection of SNPs, likelihood of an individual developing a particular disease can be predicted [7].

1.3 Background

Psychiatric disorders are one of the most common disorders prevailing today. According to the data, 26% of the people above age of 18 suffer from some particular psychiatric disorder. As no cure is available yet for any psychiatric disorder, researchers are focusing on deeper understanding of molecular aspects of these disorders and to know the pathways involved in each psychiatric disorder. In the past few years, a lot of studies have been done to reveal the genetic basis of psychiatric disorders. But all the information is scattered in literature.

Though a number of databases have been developed on neurological disorders, but they all focus mainly on neurodegenerative disorders with a central focus on Alzheimer's disease and Parkinson's disease. Very less focus has been on other psychiatric disorders. Also very few databases are based on SNPs involved in psychiatric disorders. Every database has some limitations. They are more focused on neurodegenerative disorders which are subset of psychiatric disorders and particularly towards Alzheimer's disease and Parkinson's disease. Also most of the available databases cover the diagnostic aspect rather than molecular aspect. Currently available databases are

1. NeuroDNet: it covers neurodegenerative and neuron inflammatory diseases.
2. Bipolar Disorder neuroimaging database: it includes meta – analysis and database of MRI studies of patients of Bipolar disorder
3. Alzheimer's Disease Neuroimaging Initiative (ADNI): it covers structural MRI images of Alzheimer's patients.
4. Major Depressive Disorder Neuroimaging database: it includes meta – analysis and database of MRI studies of patients of Bipolar disorder

This database will cover SNPs involved in various psychiatric disorders. This aspect has not been covered by any of the aforementioned databases as our database.

1.4 Objective

The aim of this project is to develop a database for SNPs involved in different type of psychiatric disorders and make it accessible via a web interface. The database will include all the genes involved in a particular psychiatric disorder and the mutations related to each.

1.5 Disorders Studied in the Project

There are 7 psychiatric disorders included in the study

1.5.1 Alzheimer's disease

Alzheimer's disease is the most common cause of dementia in elderly people. It accounts for ~ 50% -60% of all cases of dementia among people over age of 65. It is named after a German physician, Alois Alzheimer. He described it in early 20th century. It is a progressive neurodegenerative disorder affecting particularly the neocortex and hippocampus (brain regions associated with higher mental functions).

This disorder is characterized by

1. extracellular deposits of β-amyloid in senile plaques,
2. loss of neuronal synapses and pyramidal neurons, and
3. intracellular formation of neurofibrillary tangles.

β-amyloid in senile plaques are derived from amyloid precursor protein, encoded by APP.

Neurofibrillary tangles contain an abnormally phosphorylated form of a microtubule associated protein, encoded by tau.

These changes result in development of Alzheimer's disease which is characterized by progressive impairments of cognitive function. It is often accompanied by behavioral disturbances like depression, aggression and wandering. These behaviors are most difficult to cope with and lead to the need for institutionalization of the patient.

The major risk factor for AD is increasing age followed by family history. Other risk factors include education, gender, head trauma, memory deficit with variable severity and small volume of hippocampus. Also the estrogen replacement therapy in women has been seen to be associated with an increase in risk for AD. Early onset AD is very rare as compare to late onset AD. Generally the early onset AD is termed as familial AD. They are inherited as autosomal dominant with genetic mutations on chromosomes 1, 12 and 14.

Currently, there is no effective treatment for this disease. Currently available drugs do improve symptoms, but fail to have intense disease modifying effects. All the strategies aiming at three characteristic features of this disease require deep knowledge about molecular aspects involved in this disease. Also the current ongoing focus on therapy based on stem cells requires thorough knowledge of the genetic basis of this disease and the pathways involved [8-9-10]

1.5.2 Attention-deficit-hyperactivity disorder

Attention-deficit hyperactivity disorder is a developmental disorder characterized by the poor ability of the patient to sustain attention, impulsivity and over activity. For a person to be suffering from ADHD, both ICD-10 and DSM-IV have set criteria of following symptoms:

1. It should be pervasive i.e. symptoms must occur in two or more settings
2. It should be present before the age of seven
3. It should be persistent for more than six months
4. It must be out of keeping with developmental level
5. It must be maladaptive and significantly impairing social, academic and occupational functioning.

There is ongoing debate with respect to the etiology of the ADHD. It has been seen that a lot of factors contribute to the occurrence of this disorder. Studies have shown high rates of ADHD and behavior problems in relatives of patients, though it does not prove genetic linkage. However, studies of twins show high rate of inheritance which supports the significance of genetics.

It is very unlikely to be one single gene or one biological dysfunction responsible for ADHD.

Studies have revealed that people suffering from ADHD have certain brain regions which are being relatively under or over used. Those regions are caudate nuclei/ sub cortical striatum, the prefrontal and frontal areas, the limbic system, the posterior periventricular regions and the corpus callosum.

Also abnormal receptor sites, abnormal thyroid function, birth experiences, early life experiences, parenting and parental mental health and other psychosocial factors contribute to the development of ADHD.

There is no current acceptable biological measure of ADHD leading to difficulties with diagnosis.

Also there is no permanent treatment available for ADHD. Certain approaches like behavioral approaches, diet, social skills training, psychotherapy, counseling etc are being used [11].

1.5.3 Autism Spectrum Disorders (ASD)

ASD is a pervasive developmental disorder (PDD). It was first described by Leo Kanner in 1943. It is defined by early signs of impairments in socialization and communication and the presence of repetitive behaviors. It was first estimated to occur in 4-5 per 1000 children. Today its incidence rate has increased to 1 per 110 in the United States and 1 per 64 in the United Kingdom with almost similar incidence rate in other countries.

Cause

ASD could result from more than one cause, with different manifestations in different individuals even if they share common symptoms. It is thought that several genes may be operating together to confer susceptibility. In a small proportion of cases, various single gene disorders and chromosomal abnormalities have been reported in individuals with ASDs. Documented causes of autism include genetic mutations and/or deletions, viral infections, and encephalitis following vaccination. Therefore, cause of autism is genetic defects and/or brain inflammation. Cause of inflammation could be defective placenta, immature blood-brain barrier, the immature response of the mother to infection during pregnancy, a premature birth, encephalitis in the child after birth, or a toxic environment. It is entirely plausible that the autism phenotype might be derived from a number of different genetic components. How environmental factors interact with genetic susceptibility is as yet unclear.

Possible environmental risk factors associated with ASD are prenatal risk factors, drugs, endocrine factors, carbon monoxide, infections, immunizations etc.

Studies have revealed that people suffering from ASD show structural brain abnormalities like increase in brain weight, decrease in Purkinje cell number and developmental abnormalities of the inferior olive.

Apart from brain abnormalities, physiological, physical and psychological abnormalities have also been reported.

Autism lasts throughout a person's lifetime. There is no cure, but treatment can help. Treatments include behavior and communication therapies and medicines to control symptoms. Starting treatment as early as possible is important [12-13-14].

1.5.4 Frontotemporal dementia (FTD)

FTD is one of the most common dementia in people of age less than 65 years. It is a progressive neurodegenerative disorder of unknown etiology. It involves atrophy and neuronal loss in the frontal and temporal lobes of the brain which results in gradual and progressive decline in behavior or language.

Earlier this disease was known as Pick's disease. It is estimated that approximately 20-50% of people younger than 65 years of age suffering from dementia have FTD.

FTD syndrome has 3 distinct variants: behavioral variant FTD, semantic dementia and progressive nonfluent aphasia. All of them are characterized by the presence of behavioral and personality changes. However each variant is identified by a unique feature.

Initial symptoms of FTD are commonly misdiagnosed as primary psychiatric disorders. Studies have revealed that around 55% of FTD patients have ubiquitin – positive inclusions while 45% have tau-positive inclusions. Also presence of TAR DNA binding protein (TDP-43) has been seen in FTD patients.

Diagnosis of FTD includes a thorough family history of dementia and physical examination. Focus is given on the timing and rate of progression of symptoms, and behavioral and personality changes over the previous months or years. Clinical consensus criteria for diagnosing FTD (i.e. Neary criteria) were published in 1998. It outlines core and supportive features of behavioral variant FTD, semantic dementia and progressive nonfluent aphasia.

There is no specific cure for FTD. Treatment is focused on symptom management and support for patients, families and caregivers [15-16]

1.5.5 Obsessive compulsive disorder (OCD)

OCD is one of the more common serious mental illness which is on often chronic and potential disabling condition. It is characterized by the presence of intrusive, anxiety provoking thoughts, images or impulses along with repetitive behaviors or mental acts designed to reduce obsessional distress. It is associated with significant functional impairment, psychiatric comorbidity and compromised quality of life. It affects from 1-3% of general population around the globe.

OCD is familial. The genetics of OCD is not yet understood. Basal ganglia dysfunction has been associated with obsessive compulsive manifestations. Recent studies have revealed

association of glutamate transporter gene with early onset OCD. Environmental factors shared by children in same family contribute to symptoms score only at age 12.

Treatment of OCD involves psychotherapy, medication or both. Generally cognitive behavior therapy is useful for treating OCD [17-21].

1.5.6 Parkinson's disease (PD)

PD is the second most common age related neurodegenerative disease after Alzheimer's disease (AD). It was described by James Parkinson in 1817. It is the most common cause of parkinsonism. It results primarily from the death of dopaminergic neurons in the substantia nigra pars compacta (SNpc).

PD is a progressive disease with a mean age at onset of 55, and the incidence increases markedly with age, from 20/100,000 overall to 120/100,000 at age 70. In 95% of PD cases, disease is sporadic i.e. no genetic linkage. But in some cases it is inherited.

Symptoms

PD tremor occurs at rest but decreases with voluntary movement, so typically does not impair activities of daily living. Other symptoms are increased resistance to passive movements of a patient's limbs, bradykinesia, hypokinesia, akinesiahypophonia, drooling, micrographia etc.

The pathological hallmarks of PD are the loss of the nigrostriatal dopaminergic neurons and the presence of intraneuronal proteinaceous cytoplasmic inclusions known as 'Lewy bodies' (LBs).

Etiology and pathogenesis

The cause of sporadic PD is unknown, with uncertainty about the role of environmental toxins and genetic factors.

There are two major hypothesis regarding the pathogenesis of PD. One hypothesis posits that misfolding and aggregation of proteins are instrumental in the death of SNpc dopaminergic neurons. Other proposes that it is due to mitochondrial dysfunction and the consequent oxidative stress, including toxic oxidized DA species.

First, loss of SNpc neurons leads striatal dopamine (DA) deficiency, which is responsible for the major symptoms of PD. Second, replenishment of striatal DA through the oral administration of the DA precursor levodopa alleviates most of these symptoms. But this

treatment, after several years, cause development of involuntary movements in patients which are difficult to control and significantly impair the quality of life.

The main obstacle in the development of neuroprotective drugs is ignorance of the specific molecular events that provoke neurodegeneration in PD [22].

1.5.7 Schizophrenia

Schizophrenia is a devastating psychotic disorder which affects 1% of the population in all cultures. It impairs social and mental functioning. It affects both men and women equally, but onset is generally later in women than in men.

Risk factor

Most significant risk factor is family history. It has been observed that monozygotic twins are at high risk of developing the disease than dizygotic twins followed by first degree relative (parent, child, sibling), second degree relative (niece, nephew), third degree relative (first cousin etc.) etc.

It is a polygenic disorder in which both environmental and developmental factors plays an important role in mediating a person's possibility of becoming schizophrenic.

Symptoms

It is characterized by positive and negative symptoms.

Positive symptoms: hallucinations, paranoid delusions and voices that converse with or about the patient.

Negative symptoms: loss of sense of pleasure, flattened affects, social withdrawal and loss of will/ drive.

These changes disrupt lives of both patients and their families.

Diagnosis is done by looking for positive and negative symptoms. It is also characterized by disorganized thought, which is revealed in speech and behavior. Patients' speech is confusing and repetitive. They sometimes use words which have no relevant meaning or relationship to one another. Such behavior leads to problems in carrying out daily activities.

For a definitive diagnosis, symptoms must persist for longer period from minimum of 1month in some and at least for 6months in some cases.

Types of Schizophrenia

5 types of schizophrenia

1. Paranoid: It is characterized by a preoccupation with delusions or frequent auditory hallucinations. In this, cognitive function remains relatively well preserved.
2. Disorganized: It is characterized by disorganized speech and behavior
3. Catatonic: It has minimum of two following features – immobility, extreme negativism, excessive purposeless motor activity or peculiarities of voluntary movement
4. Undifferentiated: It occurs if none of the criteria for paranoid, catatonic and disorganized are met.
5. Residual: It is characterized by the continuous presence of negative symptoms and minimum of two attenuated positive symptoms i.e. if patient has no significant positive psychotic features.

Treatment

There is no cure of the disease. But medication can control symptoms. However, all antipsychotics have neurologic or physical side effects [23-27].

1.6 Database

A database contains data in an organized manner for any use. The data stored is generally in digital form. The term 'database' refers both to the way its users view it, and to the logical and physical materialization of its data, content, in files, computer memory, and computer data storage. It is a general definition which is independent of the technology used to create the database. Not every collection of data is database. Data must be organized in some manner such that it has a level of accuracy, availability, usability, and resilience and robustness. Because of these features there is a need for general purpose Database Management System (DBMS). It is a complex software system allowing various customizations according to user requirements and can be used to manage large and complex databases.

While database means organized collection of data, DBMS is a software system that helps in storing and updating the data, and in retrieval of information. Handling of database is quite a complex task. There is a need for a system for creating as well as managing these databases as they generally they tend to be huge and complex. DBMS provides tools for handling these databases. DBMS is package of computer software products: well-known products include the

Oracle DBMS, Access and SQL Server from Microsoft, DB2 from IBM and the Open source DBMS MySQL.

CHAPTER – 2

TOOLS AND TECHNIQUES

2.1 HTML/CSS

HTML i.e. HyperText Markup Language is the basic markup language for web pages development [28]. It provides the content that makes a webpage. It is generally without shape or form. It consists of tags (in pairs) enclosed in angle brackets.

CSS stands for Cascading Style Sheets. As name suggests, it is used to style web pages in HTML, XHTML and XML. It consists of elements like layout, colors and fonts which are used for beautification of the web page. It separates the document content; written in HTML, from document presentation by improving content accessibility, more flexibility, reduce complexity [29].

2.2 JavaScript (JS)

JavaScript is a scripting language influenced by C. It is dynamic, weakly typed. It has wide applications. It is most commonly used in web pages. It is used in animation of page elements, to provide interactive content. Apart from its use in web pages, it has use as embedded scripting language, scripting engine, application platform etc [30].

2.3 PHP

It is a server side scripting language. It is used to connect the back end and front end of a database. It is most commonly used in web development. It is generally used to create dynamic web page. It can be deployed on most web servers and can be used with relational database management systems (RDBMS). It also functions as a filter. It takes input from a file (in my project, from MySQL) and output another stream of data (here, output is HTML) [31].

2.4 MYSQL

It is the most commonly used open source RDBMS. It is written in C, C++. SQL stands for Structured Query Language. It runs as a server which provides multi-user access to a number of databases. MySQL workbench allows users to manage database design and modeling.

HeidiSQL is a full featured front end which runs on Windows. It connects to local MySQL servers in order to manage databases, tables, columns and data records [32].

2.5 WAMP SERVER

WAMP means Windows Apache MySQL PHP. It is a platform of web development under Windows. In this, a user can develop dynamic websites with the help of Apache server, PHP script language and MySQL database. It contains PHPMyAdmin which makes management of database more easy [33]. PHPMyAdmin provides a graphical user interface (GUI) for the MySQL database manager [34].

CHAPTER – 3

METHODOLOGY

This chapter gives the detailed explanation of methodology followed starting from collection of genes names and additional information till development of database using MySQL, HTML and PHP.

3.1 Psychiatric Disorders

First step was to select common psychiatric disorders to be studied. Following 7 disorders were selected:

1. Alzheimer's disease
2. Parkinson's disease
3. Autism
4. Fronto-temporal dementia
5. Obsessive compulsive disorder
6. Attention deficit hyperactivity disorder
7. Schizophrenia

After the psychiatric disorders were selected, following information was incorporated for each disorder:

1. Type of psychiatric disorder: e.g. Autism as a Developmental Disorder
2. OMIM ID
3. Inheritance
4. Etiology
5. Age range
6. Neuronal region affected
7. Characteristics of the disorder

3.2 Collection of Gene Names

Once all the psychiatric disorders were selected, then a particular disorder was selected from the list.

1. Different articles related to the selected psychiatric disorder were retrieved from PubMed using
    a. Different keywords like
        i. "Alzheimer's disease"
        ii. "Alzheimer's disease AND review"
        iii. "Genetics of Alzheimer's disease"
        iv. "Alzheimer's disease AND genes involved"
    b. Different filters
        i. Date of publishing of article
        ii. Type of article: research or review
        iii. Full article or Only Abstract available article
2. All the retrieved articles were screened manually for the relevant information.
3. All the relevant gene names were compiled under different psychiatric disorder.

3.3 Incorporation of Additional Information

Once the gene names were compiled, then following information was incorporated

1. Gene official name: from NCBI
2. Aliases: from NCBI
3. Gene location: from NCBI
4. Gene ID: from NCBI
5. Protein Name: from NCBI
6. Protein Accession No (UniProtKB/SwissProt): from NCBI
7. Gene Function: from NCBI and research/ review articles
8. Onset: from articles
9. Inheritance: from articles
10. Gene polymorphism/ SNP ID: from articles
11. Domain: from articles

12. DNA change: from articles
13. Protein change: from articles
14. Codon change: from articles
15. Type of mutation: from articles
16. Status: from articles
17. Organism: from articles
18. PMID: from articles
19. OMIM: from NCBI

3.4 Creation of Database using MySQL

1. After all the data was collected, database was created named "NidhiDB" using Wamp server.
2. Then 3 individual tables were created using Wamp server. First table included the data about the different psychiatric disorders. Second table included the data about the different genes involved in all studied psychiatric disorders. Lastly, the third table included all the polymorphisms related to the genes.

   It provided the back end of the database.

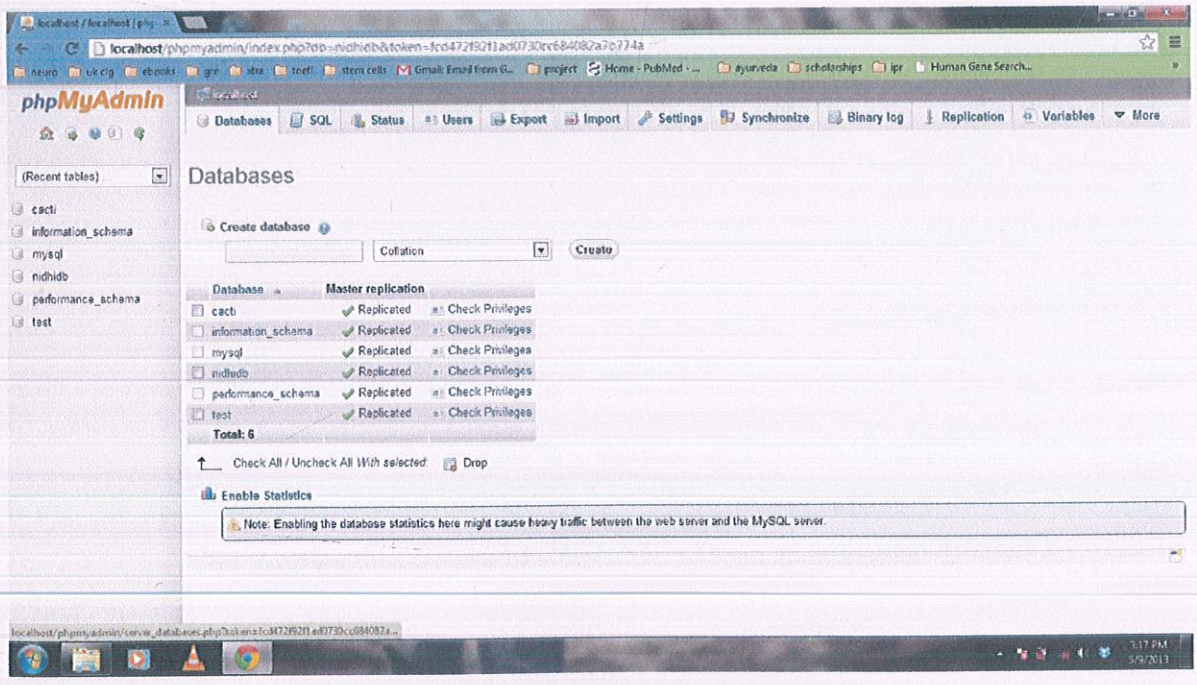

Fig. 3.1: Screenshot showing the list of databases in wamp server

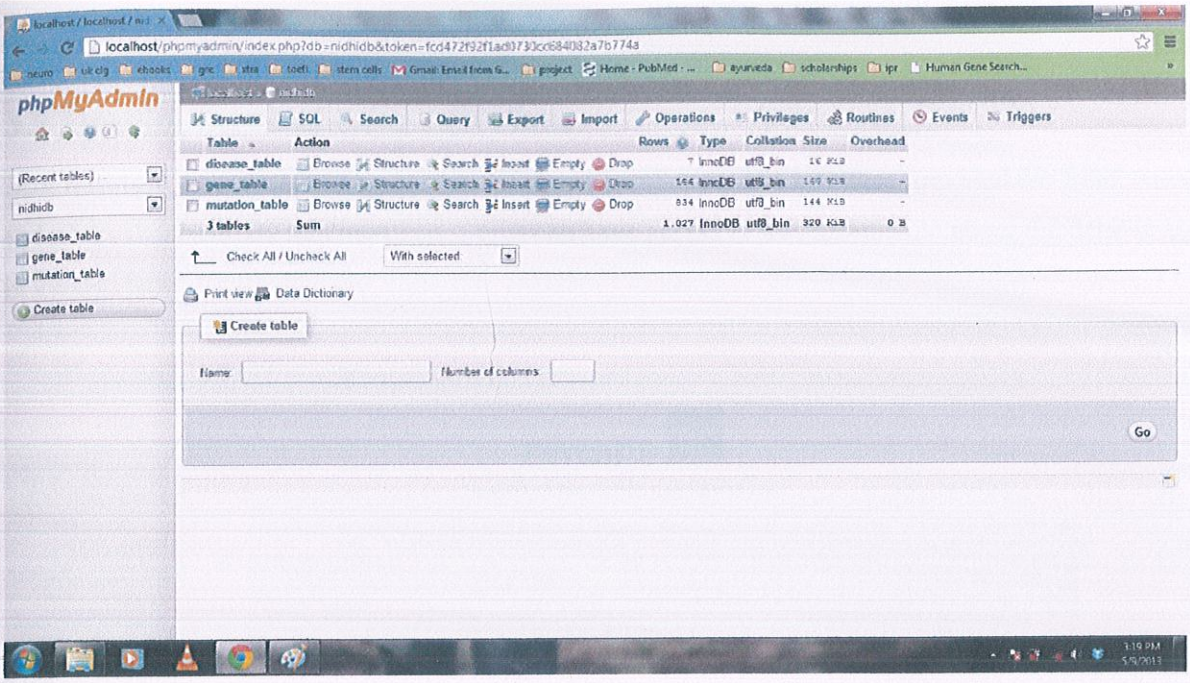

Fig. 3.2: Screenshot showing the tables in an individual database made in wamp server

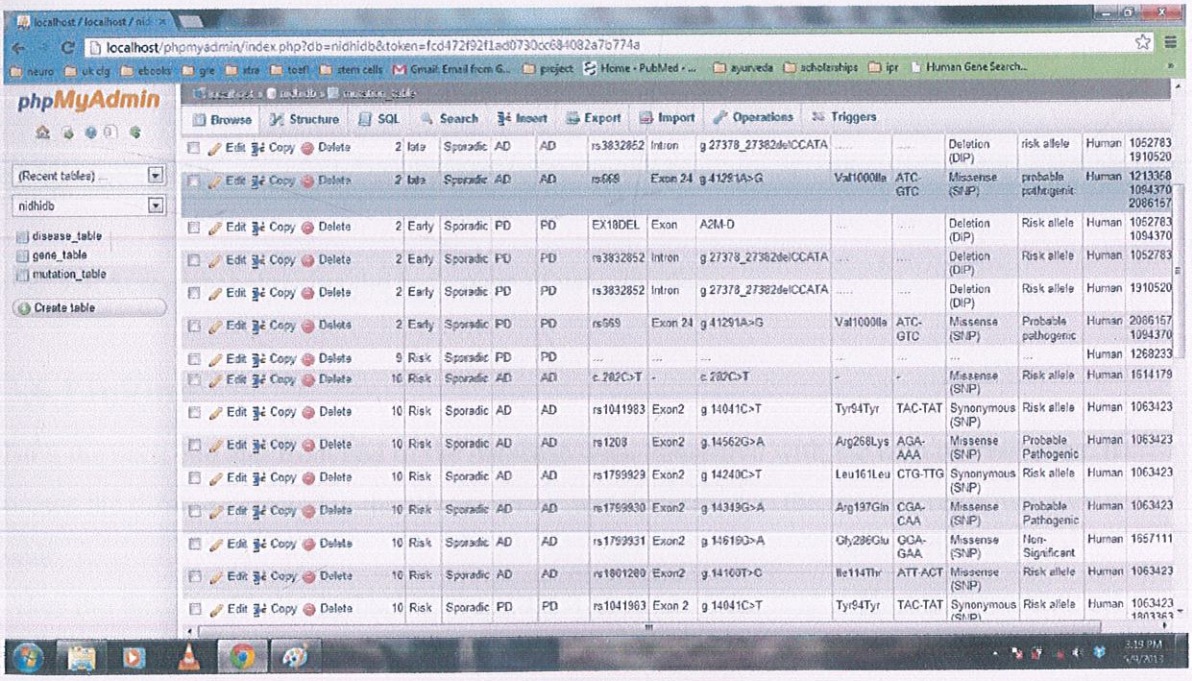

Fig. 3.3: Screenshot showing the contents of a mutation_table in an individual database i.e. nidhidb made in wamp server

3.5 Development of User Interface

User interface was created using HTML-CSS and JavaScript. The interface provided the front end of the database. By this interface, a user can have access to the information about the data in the database.

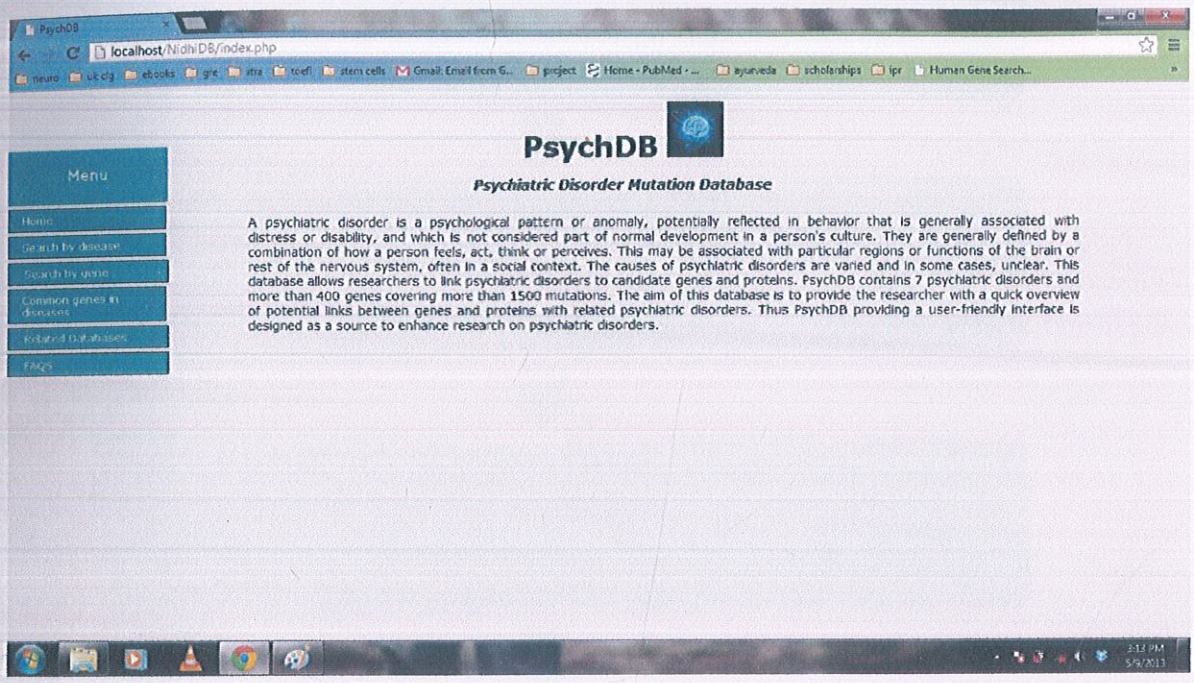

Fig. 3.4: Screenshot showing the homepage of user interface.

3.6 Linking

Both the back end and front end of the database were connected with the help of PHP code. It means the database created in the Wamp server was connected to the user interface using PHP code.

After the linking of both the back end and front end, when the user clicks on any option, all the relevant information from the database is displayed.

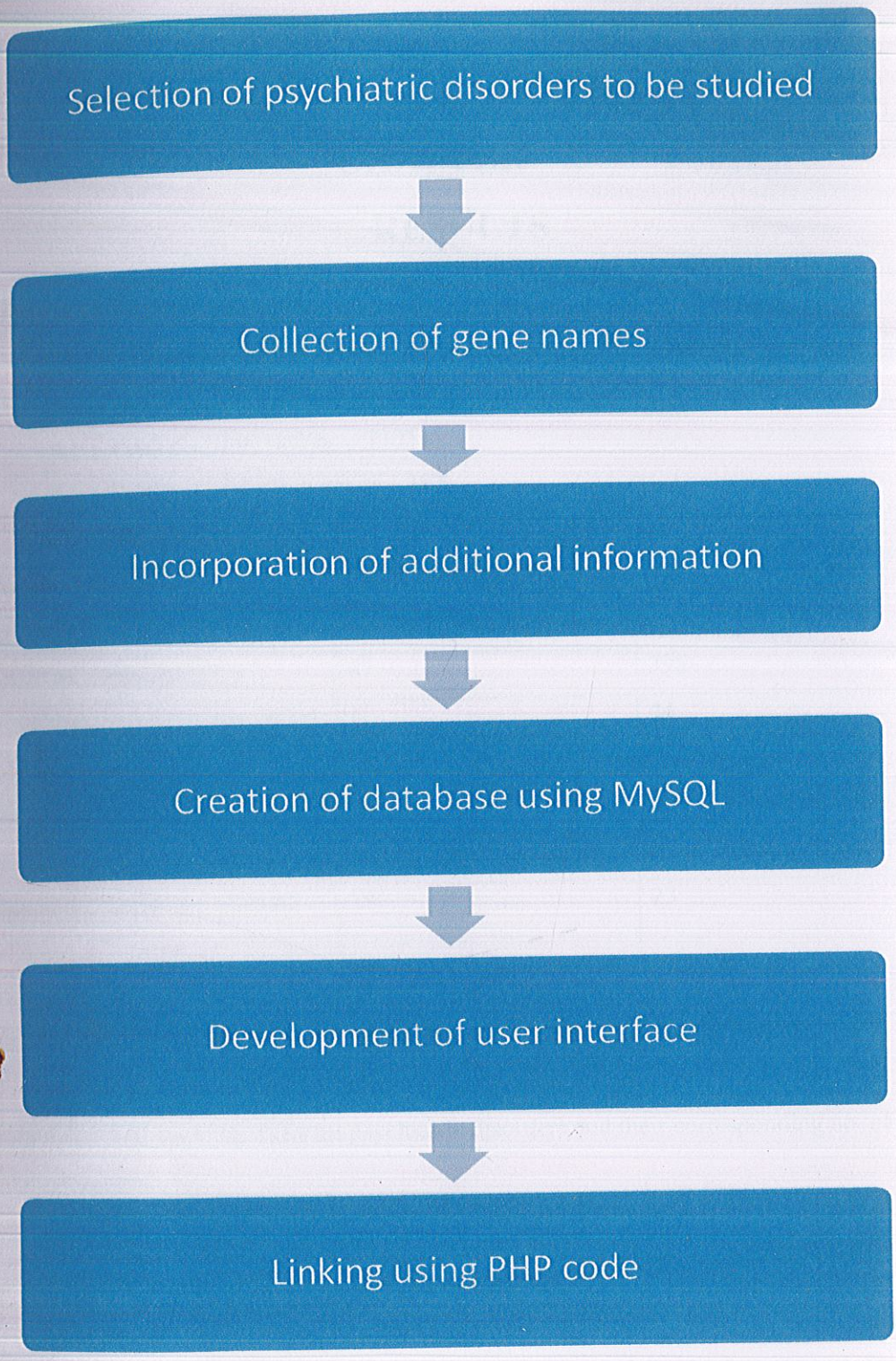

Fig 3.5: Flowchart showing methodology

CHAPTER – 4

RESULTS

4.1 Statistical Analysis

4.1.1 Total no. of diseases – 7

4.1.2 Total no. of genes – 445

4.1.3 Total no. of mutations – 1303

4.1.4 Total no. of distinct genes – 387

Disease	No. of Genes	No. of Mutations
Alzheimer's Disease (AD)	105	369
Parkinson's Disease (PD)	87	398
Fronto temporal dementia (FTD)	7	44
Autism	173	360
Attention deficit hyperactivity disorder (ADHD)	30	69
Obsessive compulsive disorder (OCD)	12	23
Schizophrenia	31	40
Total	445	1303

Table 4.1: Table showing different psychiatric disorders and their corresponding no. of genes and mutations

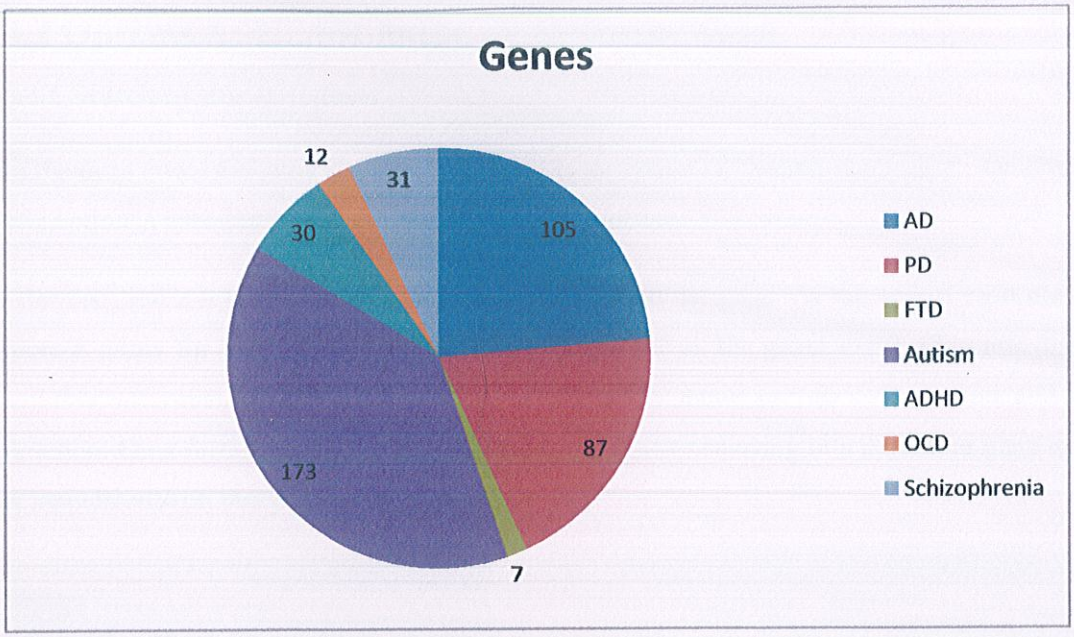

Fig. 4.1: Pie Chart showing diseases and no. of genes involved in the disease

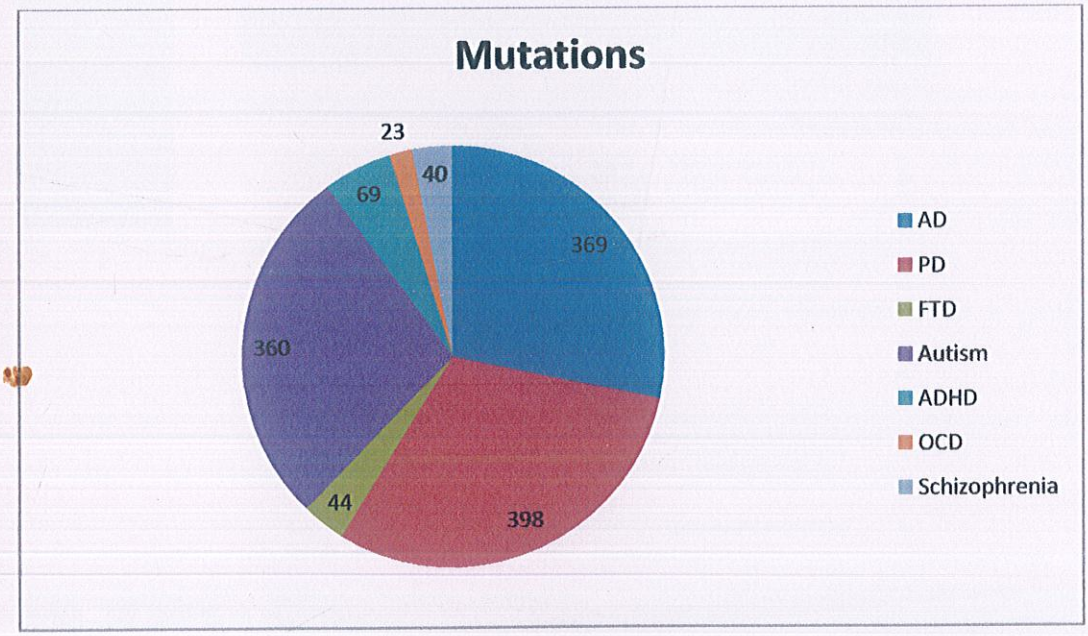

Fig. 4.2: Pie chart showing diseases and mutations contributing to the disease

4.2 Options Available in the Drop down Menu

4.2.1 Search by disease option

In the drop down menu on the interface, there is an option of 'Search by disease'. On clicking this option, a user can see all the diseases in the database.

User can find a brief description about the diseases on the page. At the end of each disease, there is a link for the genes. On clicking it, user can see all the genes involved in that disease and their information like gene id, gene location, protein name, protein accession no. and gene function. On a further click, one can see polymorphisms occurring in a particular gene which is associated with that particular disorder.

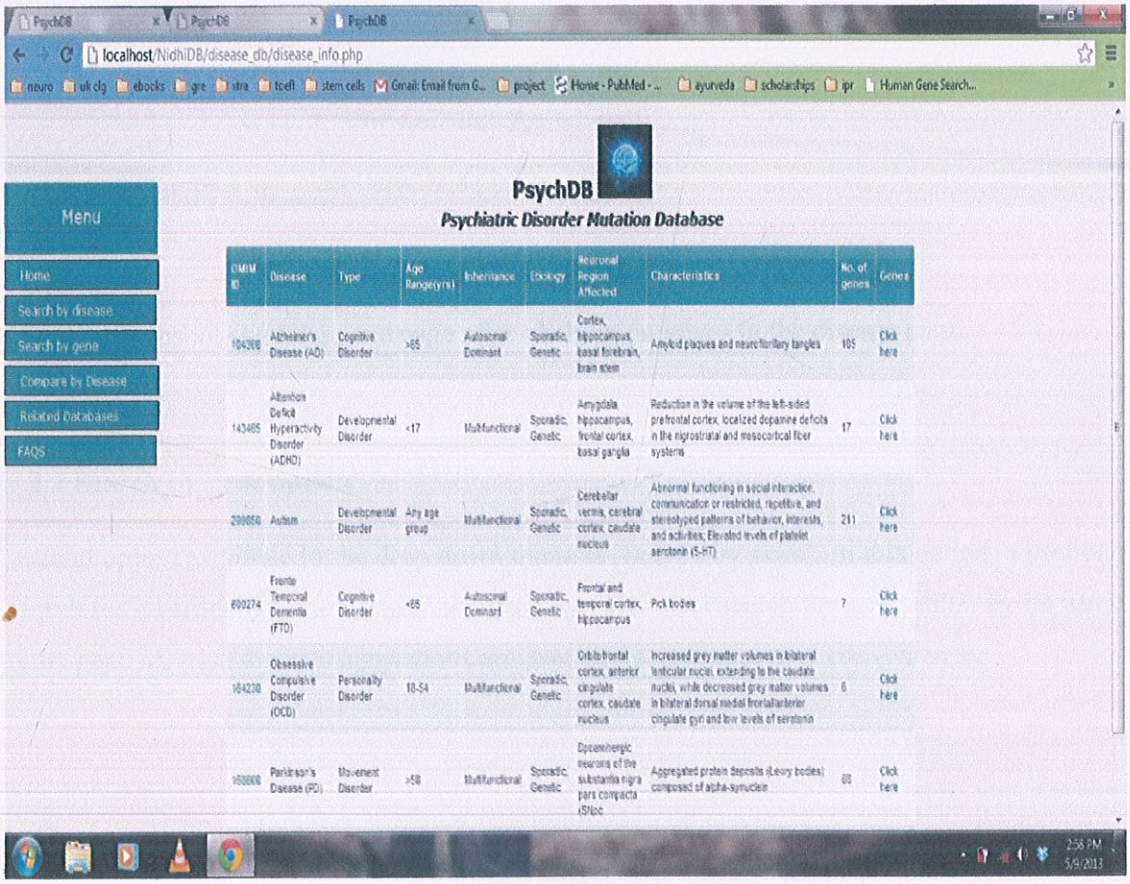

Fig. 4.3: Snapshot showing disease page of the database.

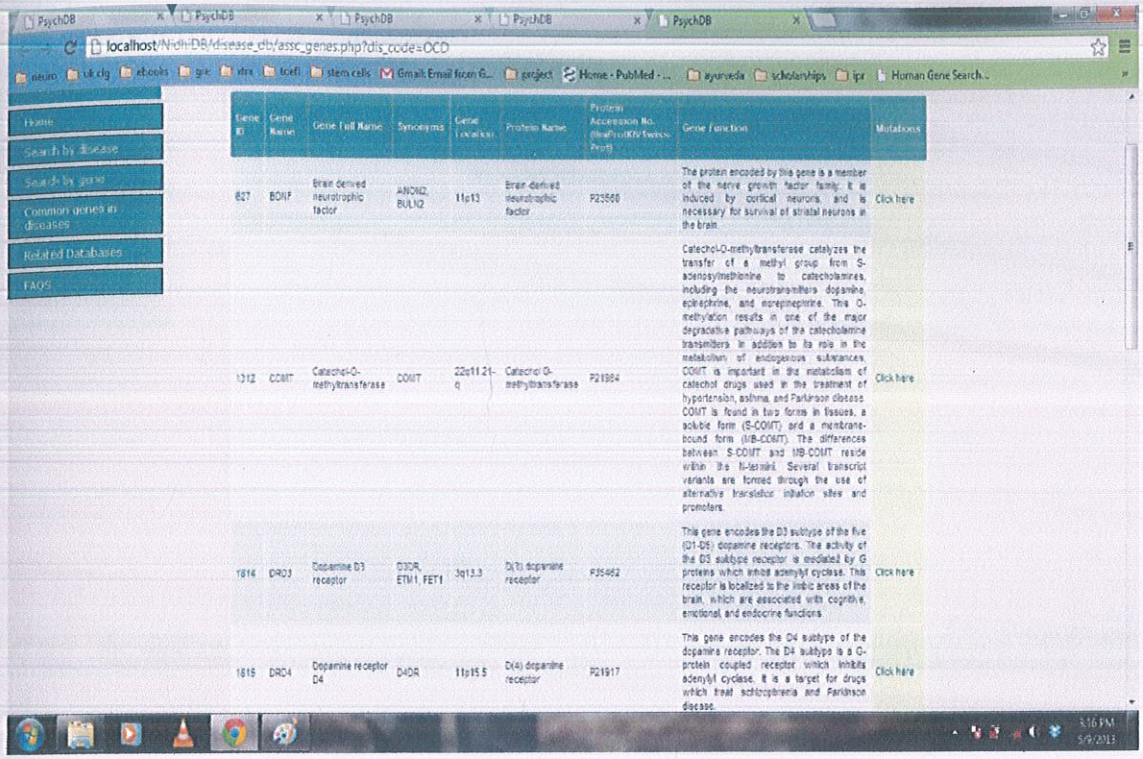

Fig. 4.4: Snapshot showing gene page after clicking on genes in the disease page.

4.2.2 Search by gene option

Second option available in the drop down menu is 'Search by gene'. In this option, a user can search for a particular gene listed in the database. User can search the gene either by its name or by gene id. Also the autosuggestions are provided to enhance user convenience.

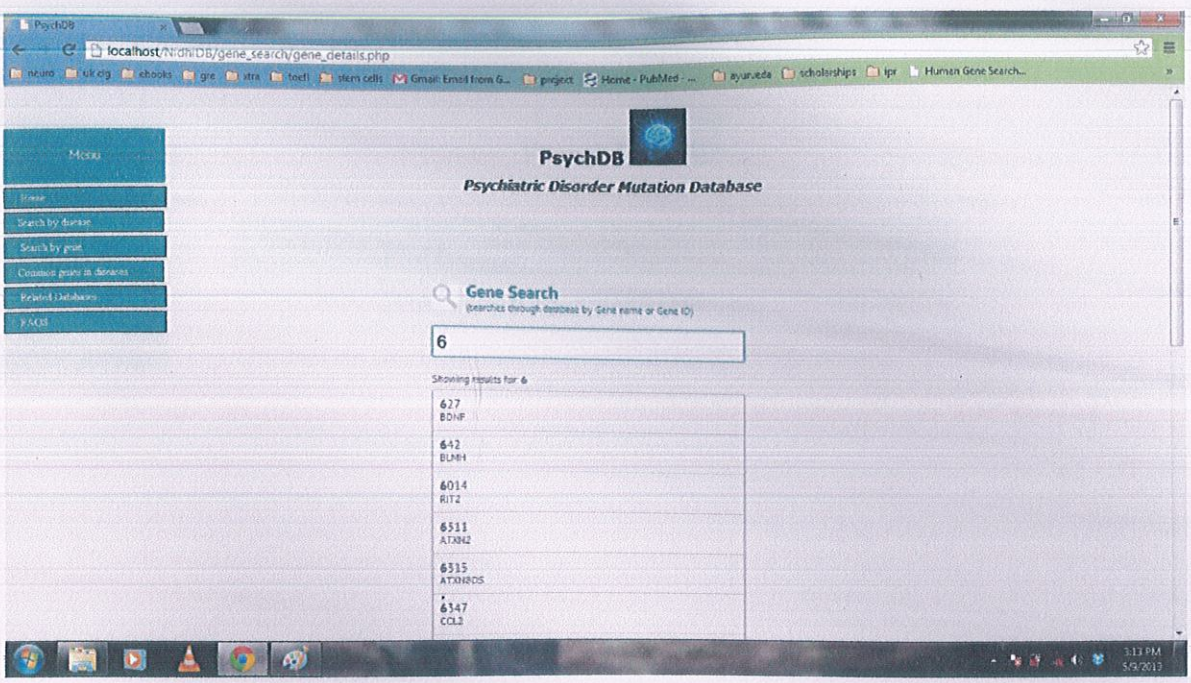

Fig. 4.5: Snapshot showing gene search option through gene id.

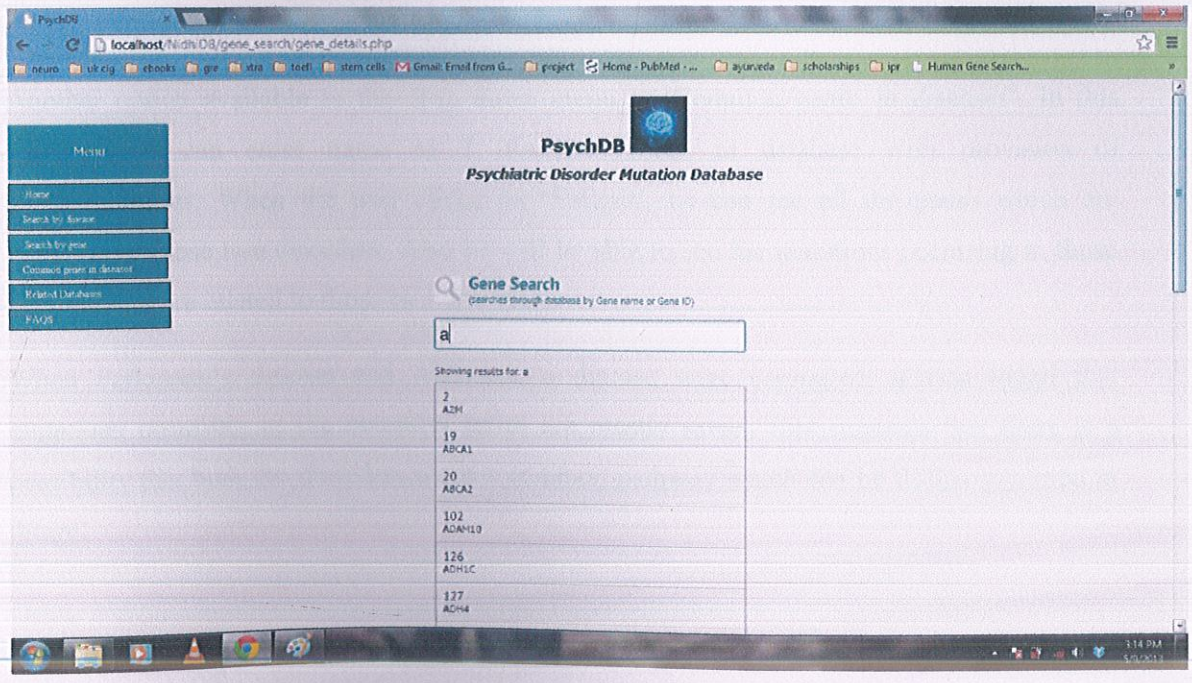

Fig. 4.6: Snapshot showing gene search option through gene name.

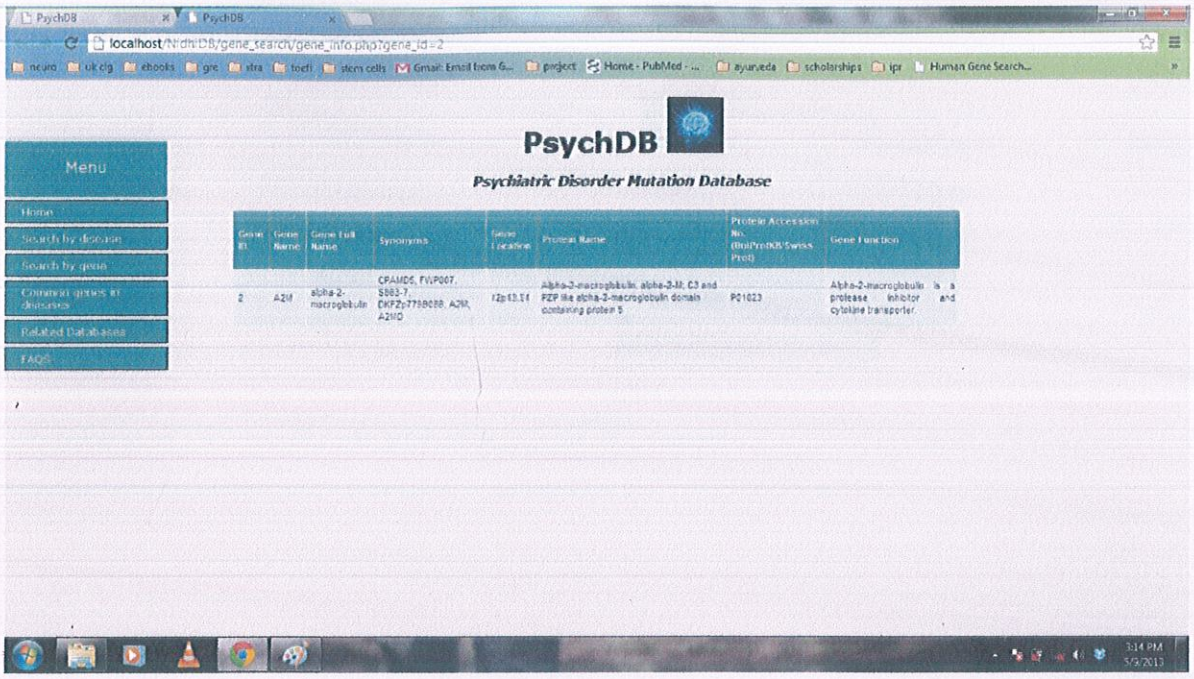

Fig. 4.7: Snapshot showing result when user clicks on gene search.

4.2.3 Common genes in diseases option

Another option available in the drop down menu is 'Common genes in diseases'. In this option, user can enter name of 2 disorders listed in database with provision of autosuggestions. When the user clicks on 'Submit', he can see all the genes which are common in those two disorders. Also he will be able to see the mutations occurring in those genes which are related to those two disorders.

When Parkinson's disease and Alzheimer's disease were compared, it was found that mutations occurring in the common genes are mostly same. This suggests that there is a possibility that both the disorders share a common pathway which can be further explored in future.

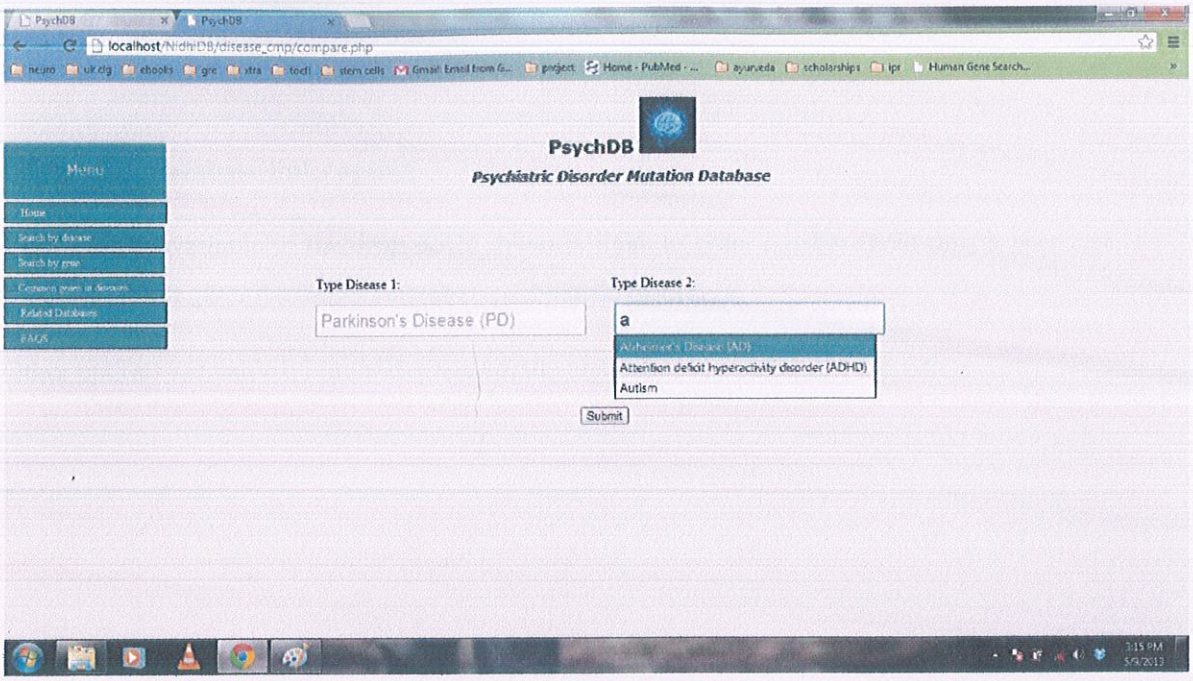

Fig. 4.8: Snapshot showing 'Common genes in disease' option page.

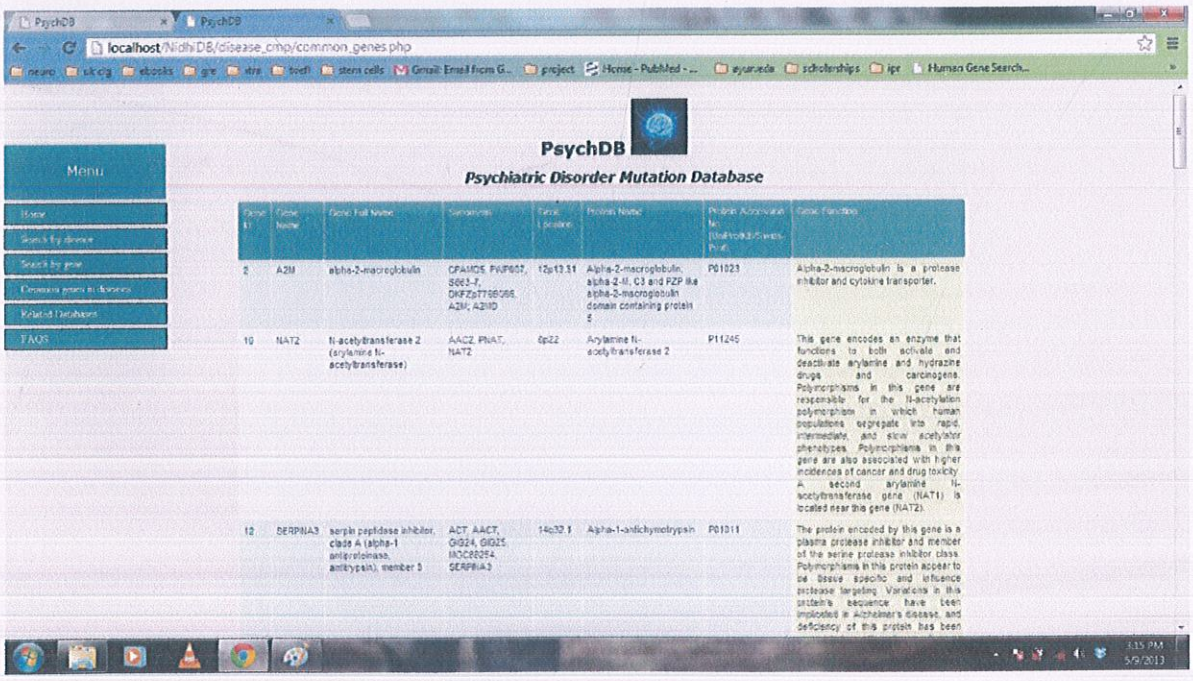

Fig.4.9: Snapshot showing all the common genes in the two disorders submitted in the query.

4.2.4 Other database links option

Final option available in the drop down menu is links to other databases. In this, a user can find links to all other databases related to psychiatric disorders.

Other options available on the web page are the contacts of contributors and FAQs.

CHAPTER – 5

APPLICATIONS OF THE PROJECT

PsychDB describes a comprehensive repository of information about molecular aspects of different psychiatric disorders. It is hoped to serve as a useful resource to the academic and research community. In this, a user will be able to look for all the SNPs occurring in any gene responsible for a particular disorder. By analyzing the SNPs, one can study its affect on a particular protein; how a mutation alters the structure of a protein and its interaction with other target proteins. One can compare the functionality of wild protein and mutated one. This database will allow the user to study the effects of multiple mutations on a particular protein rather than one single SNP. In addition, user can compare two disorders and can analyze the data obtained by different researchers at one site.

CHAPTER – 6

CONCLUSION

We have developed a database named PsychDB which will allow the users to search for different psychiatric disorders available in the database. It will provide all the genes involved in a particular disorder and the polymorphisms related to that gene of a disorder. It will also include other information related to that gene like its function etc. Apart from the above mentioned information, database will also include relative literature and documents for reference through PubMed. There is no cure available for the psychiatric disorders yet. Researchers have found that one of the causes of the psychiatric disorders is genetic. They are looking for the mutations occurring in different genes responsible for causing such disorders so that they can find how each mutation is affecting the normal pathway leading to the development of disorder. As the required information is scattered in the literature, so there is a need to refer to databases that could provide such information in an organized manner. Though there are several databases available today but none of them provide all the information. Hence for this purpose and to add consistency, we have developed a database which provides a handful of information on different psychiatric disorders. It will help students, researchers and medical professionals to obtain the desired information by single query. They can search for a specific gene and can obtain all the information relevant to that gene. They can also search a particular disorder and can look for all the genes involved in that disorder and the mutations related to it. They can further look for genes common in any two disorder and the mutations involved in each.

Database is available for research and academic use at
http://juit.ac.in/attachments/PsychDB

In future, we aim to add more psychiatric disorders to the database. We also aim to update the database regularly by adding more genes and SNPs to the existing psychiatric disorders.

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