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Abstract

Schizophrenia is a complex neuropsychiatric disease with a global prevalence of 1% in the general population. It is caused by a combination of genetic, environmental factors and age of onset is in adolescence where it occurs early in males (late teens to early twenties) compared to females (late twenties to early thirties). Due to a mental disorder its symptoms are of significance and importance. There are three types of symptoms in schizophrenia positive, negative and cognitive symptoms. The positive symptoms refer to delusions, hallucinations the negative symptoms involve lack of motivation, alogia (diminished speech) and anhedonia (absence of pleasure) whereas cognitive symptoms are related to deficits in learning, attention and memory. The pathophysiology of schizophrenia is mostly restricted to defects in neurotransmitter system such as dopamine, glutamate, serotonin and γ-aminobutyric acid (GABA). So, the current treatments of antipsychotics are aimed at manipulating the neurotransmitters but the treatment is not effective and leads to multiple side effects such as extrapyramidal symptoms and weight gain. There is a need to find new therapeutic targets using in silico and in vivo methods by investigating current environmental and genetic factors of schizophrenia.

KEYWORDS: Schizophrenia, Delusions, Hallucinations, Anhedonia, Dopamine, Antipsychotics.

Discussion

The already published data indicates that schizophrenia is a multifactorial disease.

It involves both genetic and environmental factors.

Schizophrenia diagnosis is based on Diagnostic and Statistical Manual-5 (DSM-5) which is questionnaire based.

The current treatments lack efficacy and only provide partial relief.

There is an urgency to find new therapeutic targets.

So this study is a preliminary study to explore genetic candidates as new therapeutic targets of schizophrenia.

Methods and Materials

1. Literature mining for the 'Gene of Interest'.
2. Constructing pathway on the basis of literature abstraction.
3. Analyzing the constructed pathway using different bioinformatics tools.
4. The pathway analysis enables us to identify new therapeutic targets for schizophrenia.

S.NO	Dopamine Pathway	Function
1.	Nigostriatal	Movement and sensory stimuli.
2.	Mesolimbic	Pleasure and reward seeking behavior, addiction, emotion, behavior.
3.	Mesocortical	Cognition, memory, attention, emotional behavior learning.
4.	Tuberoinfundibular	Control of the hypothalamic pituitary endocrine system, inhibition of prolactin secretion.

Table 1. Available drugs of schizophrenia and their side effects.

Drug	Weight Gain	Extrapyramidal Symptoms
Typical Antipsychotics (First-Generation Antipsychotics)		
Chlorpromazine (Thorazine)	++	+++
Fluphenazine (Prolixin)	+	++++
Haloperidol (Haldol)	+	++++
Perphenazine (Trilafon)	+	++++
Thioridazine (Mellaril)	+	+++
Thiothixene (Navane)	+	++++
Atypical Antipsychotics (Second-Generation Antipsychotics)		
Aripiprazole (Abilify)	+	+
Asenapine (Saphris)	+	++

Results

In this study schizophrenia pathophysiology is investigated and different genetic candidates are analyzed to find new therapeutic targets.

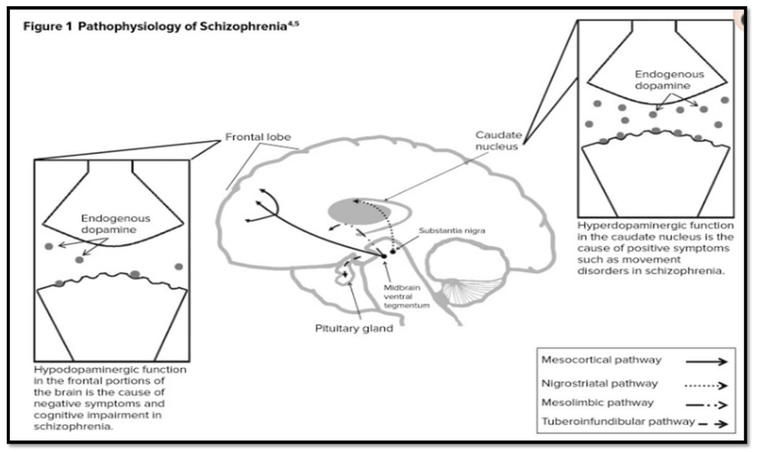
The list of genetic candidates were retrieved through literature.

The most cited, multilateral gene candidates were explored to find their association with schizophrenia.

The gene candidates having critical function, role in schizophrenia pathophysiology were analyzed.

The results were compiled for Bioinformatic Analysis and later was compared with available wet lab data to draw conclusions.

Figure 1. Different pathways involved in the pathophysiology of schizophrenia.



Conclusions

Overall, I would like to conclude that considering schizophrenia as a neuropsychiatric disease which affects 1% general population.

The attention, urge required to combat this disorder is lacking so a determined mindset and innovative approach is required.

This study would serve as stepping stone to move towards more advanced research.

The patients of schizophrenia in our society need care, affection and as researchers our efforts should be directed to alleviate their misery.

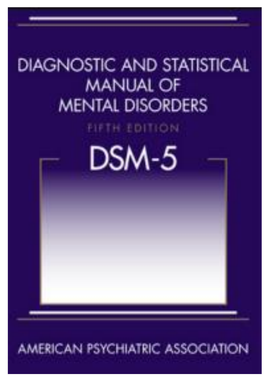


Figure 2. Diagnosis of schizophrenia DSM-5.

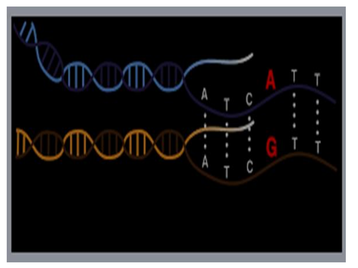


Figure 3. Genetics of schizophrenia.

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