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Investigations of Epilepsy

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Abstract

Epilepsy is a disorder of brain characterized by an ongoing liability to recurrent epileptic seizures [1]. Studies show that one percent of the approximately 160 million population of Pakistan has Epilepsy[2]. There are different underlying causes of epilepsy, one of them is the Genetic based cause of this brain disorder. Many Genes have been reported to contribute in Epilepsy. Targeting these Genes, medical scientists have done enormous research on this subject. To know the underlying cause of the mechanism of Epilepsy, the Investigation of Genetic Contributions in Epilepsy is required. Our work is the act or process of furnishing critical commentary of those Genes that plays an important role in causing Epilepsy. Mutations are the actual cause of any genetic disorder. We have examined these mutations in different genes and we have taken into account the number of frame shifts in the genes and also tabulate them. Functional regions present in genomic sequences also known as the Conserved regions and are identified through different bioinformatics software to show their contribution in Epilepsy.

Keyword: *Epilepsy*

Introduction

The word epilepsy is derived from the Greek word for "attack." People once thought that those with epilepsy were being visited by demons or gods [3]. Two decades ago, 78% of people with epilepsy in Pakistan would go untreated. Wrong perceptions of illness and deeply rooted cultural and religious beliefs have led to stigmatization, marginalization, and negative treatment-seeking behavior and attitudes [4].

Epilepsy is basically a brain disorder in which clusters of nerve cells or neurons system in the brain behave abnormally and sometimes generated unwanted signal. In epilepsy, the actual pattern of neuronal activity becomes abnormal, causing strange sensations, emotions, and behavior or sometimes convulsions, muscle spasms, and loss of consciousness. There are so many possible causes behind the mental disorder (Epilepsy). Anything that disturbs the normal pattern of neuron activity from illness to brain damage to abnormal brain development can lead to seizures. Epilepsy may develop because of an abnormality in brain wiring, an imbalance of nerve signaling chemical called neurotransmitters, or some combination of these factors. Having a seizure does not necessarily mean that a person has epilepsy [5]. Only when a person has had two or more seizures is he or she considered to have epilepsy [5].

Seizures

A seizure is the result of a sudden electrical surge in the brain. This causes the brain's messages to become temporarily halted or mixed up. The type of seizure a person has depends on the area of the brain where this activity occurs [6].

Mutations That Affect Functions:

- Loss-of-function mutations are the result of gene product having less or no function.
- Gain-of-function mutations change the gene product such that it gains a new and abnormal function.
- Dominant negative mutations (also called antimorphic mutations) have an altered gene product that acts antagonistically to the wild-type allele. These mutations usually result in an altered molecular function [7]
- Lethal mutations are mutations that lead to the death of the organisms which carry the mutations.
- A back mutation or reversion is a point mutation that restores the original sequence and hence the original phenotype[8]

Methodology

This detailed study is based on the utilization of

online database available at NCBI (National Centre of Biotechnology Information) for accessing relevant Genes, SNPs and Proteins. 10 genes were selected from the database on the basis of minimum SNPs reported. Our center of cram was the point mutations (non synonymous mutations) that occur enormously to cause disease. These mutations are often found to be the major contributors of functional abnormality. SNPs have a great significance in functional analysis of genes. The noticed SNPs for selected genes has been tabulated to study the variations in conserved non coding regions that lead to changes in the compliment of transcribed sequences. Bioinformatics software Motif search was used to identify the conserved regions. We searched a protein query sequence against Motif Libraries to find the functional sites.

Results & Discussion

The total of 10 genes was observed with their respective proteins to cover for the functional sites. Table of missense mutations reported 55 mutations that set out our track and remain within this domain. Out of those 55 mutations, we found 22 to be functional. This shows that if the mutation occurs within any of these sites, it leads to Epilepsy. Following software's are utilized for functional analysis

- Automotif
- Swiss Model
- Swiss PDB Viewer

Table 1 Epileptic Genes searched

S.NO	Genes
1	ATP6AP2
2	GABRD
3	JRK
4	SRPX2
5	CSTB
6	CHRNB2
7	SCN1B
8	NHLRC1
9	MEF2C
10	KCTD7
	Total

Table 2: Summary table for Dysfunction

Genes	Mutation Leads to
ATP6AP2	Mental retardation and epilepsy points
GABRD	Generalized epilepsy with febrile seizures
JRK jerky homolog(Mouse)	Childhood Absence Epilepsy (CAE)
SRPX2 sushi-repeat containing protein, X-linked 2	Bilateral perisylvian polymicrogyria, rolandic epilepsy, speech dyspraxia and mental retardation
CSTB cystatin B (stefin B)	Progressive myoclonic epilepsy (EPM1)
CHRNB2 cholinergic receptor, nicotinic, beta 2 (neuronal)	Autosomal dominant nocturnal frontal lobe epilepsy.
SCN1B sodium channel, voltage-gated, type I, beta	Generalized epilepsy with febrile seizures plus, Brugada syndrome 5,
NHLRC1 NHL repeat containing 1	Progressive myoclonic epilepsy type 2 (EPM2).
MEF2C myocyte enhancer factor 2C	Severe mental retardation, stereotypic movements, epilepsy, and cerebral malformation
KCTD7 potassium channel tetramerisation domain containing 7	Progressive myoclonic epilepsy-3

Table 3 Number of observed Mutations with respect to genes

S.NO	Genes	No. Of Missense mutations
1	ATP6AP2	4
2	GABRD	5
3	JRK	7
4	SRPX2	5
5	CSTB	2
6	CHRNB2	3
7	SCN1B	15
8	NHLRC1	8
9	MEF2C	4
10	KCTD7	
	Total	**55**

Table 4 Mutations in Functional Regions

S.NO	Genes	No. Of Functional region Mutations
1	ATP6AP2	4
2	GABRD	3
3	JRK	1
4	SRPX2	3
5	CSTB	0
6	CHRNB2	1
7	SCN1B	7
8	NHLRC1	1
9	MEF2C	1
10	KCTD7	1
	Total	**22**

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