Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 4 [2] January 2015: 28-31

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD
Global Impact Factor 0.533
Universal Impact Factor 0.9804

ORIGINAL ARTICLE

Evaluation of DISC1 gene rs3738401 polymorphism in Iranian patients affected by Schizophrenia and normal individuals

Narmin Mokarizadeh[1]*, Shima Rezaii afarmejany[2], Mohadeseh Nemati [1,3],Khadijeh Azarhoosh[4], Venus Haghshenas[5]*

[1] Department of Biochemistry, School of Medicine, Urmia University of Medical Science, Urmia, Iran
[2] Department of Biochemistry, Islamic Azad University of Ardabil, Iran
[3]Student research committee, Urmia University of Medical Science, Urmia, Iran
[4]Faculty of biology sciences, Islamic Azad university of Tonekabon,Iran
[5] Aria medical diagnostic laboratory, Sanandaj ,Iran
***Corresponding Author's** Email: v.haghshenas@yahoo.com

ABSTRACT

Schizophrenia is a chronic, harsh, and disabling brain disorder that has affected people during history. Schizophrenia affects men and women equally. It happens at similar rates in all ethnic groups all over the world. Diagnosis is based on observed manners and reported experiences. In this study, the DISC1 gene rs3738401 polymorphism in Iranian patients affected by Schizophrenia and individuals was investigated. The present investigation was conducted including number of 71 Iranian patients suffering from Schizophrenia and 140 normal subjects by employing ARMS-PCR method. To conclude, the information and statistics received from this study was analyzed by SPSS software.To sum up, the end outcome of current study explains considerable relation between DISC1 gene rs3738401 polymorphism in Iranian patients affected by Schizophrenia and individuals. It could be an important genetic predisposition feature.
Keywords: DISC1, rs3738401, Schizophrenia,gene polymorphism

Received 20.09.2014 **Revised 01.11.2014** **Accepted 08.12.2014**

INTRODUCTION

Schizophrenia is a mental illness frequently characterized by unusual social manners and failure to identify what is real. People with this disorder may take notice of voices other people don't hear. This could terrify individuals with the sickness and cause them to become withdrawn or extremely agitated. They may suppose other people are reading and controlling their thoughts, or plotting to hurt them [1,2].

Sometimes individuals who have schizophrenia seem absolutely okay until they discuss what they are really thinking. People who suffering schizophrenia might not sound right they talk. They might sit for long time without moving or talking [3].

Nobody has been capable to pinpoint one particular cause. Experts believe a number of factors are commonly involved in contributing to the onset of schizophrenia. Evidence does declare that genetic and environmental factors normally work together to bring about schizophrenia [4]. Evidence pointed out that the diagnosis of schizophrenia possesses an inherited aspect, nonetheless can also be significantly influenced by environmental triggers.

Disrupted in schizophrenia 1 is a protein that is determined by the *DISC1* gene in humans [5]. A number of surveys have exposed that unregulated expression or distorted protein organization of DISC1 may predispose persons to the development of schizophrenia, clinical depression, bipolar disorder, and other psychiatric situations. [6]. The cellular functions that are disrupted by permutations in DISC1, which direct to the development of these disorders, have yet to be obviously defined and are the issue of present ongoing study. In coordination with a wide range of interacting partners, DISC1 has been publicized to participate in the regulation of cell proliferation, differentiation, migration, neuronal axon and dendrite result, mitochondrial movement, and cell-to-cell adhesion [7].

The DISC1 gene is located at chromosome 1q42.1 and overlies with DISC2 open reading frame [8]. Multiple DISC1 isoforms have been acknowledged at the RNA level, including a TSNAX-DISC1 Trans gene splice variant, and at the protein rank. Of the isolated RNA isomers, 4 have been confirmed to be translated that is extended form (L), long variant isoform (Lv), tiny isoform (S), and particularly miniature isoform (Es).

Human being DISC1 is transcribed as two major splice variants, L shape and Lv isoform. The L and Lv transcripts use distal and proximal join sites, correspondingly, in exon 11. The L and Lv protein isoforms differ by just 22 amino acids within the C-terminus. Schizophrenia, Bipolar disorder and schizoaffective disorder are usual psychiatric sickness with elevated heritability and changeable phenotypes. The *Disrupted in Schizophrenia 1* (*DISC1*) gene, on chromosome 1q42, was initially revealed and connected to schizophrenia in a Scottish kindred carrying a balanced translocation that disrupts *DISC1* and *DISC2.* [9]

The present survey was done including a number of 71 Iranian patients suffering from Schizophrenia disease and 140 normal subjects by utilizing ARMS-PCR system. Finally, the facts received from this study were analyzed by SPSS software.To be brief, the end result of present study shows substantial relation between DISC1 gene rs3738401 polymorphism in Iranian patients affected by Schizophrenia and individuals. It could be a significant genetic predisposition factor.

MATERIAL AND METHODS

This research was performed on 71 patients with Schizophrenia and 140 healthy controls. The patient's samples were casually extracted from Hazrat-e-Abolfazl Mental Rehabilitation Center, Hamadan, Iran. The control group was selected from random participants whose health was established by medical diagnostic.

DNA extraction and PCR Reaction

Genomic DNA from venous blood samples were isolated using DNA Extraction Kit PGS (Model: PGS0051) in accordance with manufacturer's instructions.DNA were quantified with the NanoDrop technology (Thermo Scientific / NANODROP 1000 Spectrophotometer).The DISC1 gene rs3738401 polymorphism genotyping was performed base on the amplification-refractory mutation sequencing (ARMS) assay. The Thermal cycling conditions for ARMS-PCR were the following. Figure1 Utilizing the BIOER TECHNOLLOGY CO .LTD. (Model: TC-24/H.b) For The PCR We Used 20 µL Sample: 1 µL Forward Primer, 1 µL Reverse Primer, 6 µL Diluents'Water, 2 µL DNA 50 ng/ml, 10 µL Master Mix Sequence of Primers was 5'- GTT CCT TTC CCC AGC AGT G -3' ´as forward primer,5´-5'-AGA ATG CAT GTC ACG CTC T -3'as reverse normal primer and 5'-AGA ATG CAT GTC ACG CTC C -3'as reverse mutant primer. Human beta-globin gene amplified in each reactions using specific primers, 5'-ACACAACTGTGTTCACTAGC-3' as forward and 5'-CAACTTCATCCACGTTCACC-3' , as internal control as well and the PCR product was run on a 2% Arose gel in 0.5× TBE buffer and visualized on a Gel Documentation System using Gel Red dye.

PCR program used for DISC1 gene rs3738401 polymorphism:

cycle	temperature(Celsius)	Time
first	95	7 Minutes
Two to thirty-five	94 59 72	1minuteand15seconds 55Seconds 30seconds
thirty-six	72	5Minutes

Gel Electrophoresis

The electrophoresis was carried out using 1%Gel Redstained agarose gel, at 80V for 35 min We Use Horizontal Electrophoresis Cell (Model: JY-SPAT) with TBE Buffer ($_P$H=8.3) , Ladder Were Used 50bp DNA Ladder (Jena Bioscience) After electrophoresis, the amplified PCR products were Perceive under U. V. light

Statistical analysis

Statistical analyses were conducted using with the SPSS software (Statistical Package for Social Sciences) version18. Chi- square test ($\chi 2$), was used to check the association between two categorical variables or even to detect difference between several proportions. Pearson chi-square was used to investigate the connection involving the DISC1 gene rs3738401 polymorphism and Schizophrenia.

RESULTS

We genotyped and analyzed 71 patients with Schizophrenia, and 140 healthy controls younger than 65 years, for the DISC1 gene rs3738401 polymorphism. rs3738401 polymorphism frequencies were in equilibrium in patients and controls. Patients showed an extensively increased frequency of the rs3738401 polymorphism allele compared with controls. Thus the rs3738401 polymorphism allele would confer a slightly increased risk of developing late onset Schizophrenia.

Table1: Genotype Table of DISC1 gene rs3738401 polymorphism:

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Genotype * Group	211	100.0%	0	.0%	211	100.0%

Genotype * Group Cross tabulation

Count

		Group		
		PATIENTS	CONTROL	Total
Genotype	GG	22	0	22
	GT	26	80	106
	TT	23	60	83
Total		71	140	211

The results of genotyping are depicted in Table1: The following genotypes were identified for DISC1 gene rs3738401 polymorphism.

Table2: ALLEL Table of DISC1 gene rs3738401 polymorphism:

		Allele				Total
		G		T		
GROUP	Case	76	66%	44	38%	120
	Control	157	89%	7	7%	164
Total		233		51		284

Table 2 showed that there were significantly correlation between DISC1 gene rs3738401 polymorphism and Schizophrenia. Therefore, DISC1 gene rs3738401 polymorphism may be a genetic predisposing factor for Schizophrenia in Iranian population.

Table3: Chi- square test ($\chi 2$) for analyzing DISC1 gene rs3738401 polymorphism:

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	45.992[a]	2	.000
Likelihood Ratio	50.525	2	.000
Linear-by-Linear Association	19.935	1	.000
N of Valid Cases	211		

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7.07.

DISCUSSION

The evidence exposed in the article confirms that DISC1 gene rs3738401 polymorphism plays a vital role in Schizophrenia of Iranian patients. In accordance with this, an increased frequency of the allele among patients with Schizophrenia has been seen.

By analyzing a group of Iranian patients, it is understood that the DISC1 gene rs373401 has been associated with this disorder. As a result DISC1 gene rs3738401 polymorphism is actually a noteworthy

genetic tendency factor for in Iranian Schizophrenia patients. Therefore, DISC1 gene rs3738401 polymorphism may be a genetic predisposing factor for Schizophrenia treatment in Iranian population.

REFERENCES

1. Jablensky A, Sartorius N, Ernberg G, et al. (1992). "Schizophrenia: manifestations, incidence and course in different cultures. A World Health Organization ten-country study". Psychological Medicine Monograph Supplement 20: 1–97.
2. Antipsychotics for schizophrenia associated with subtle loss in brain volume". ScienceDaily. February 8, 2011. Retrieved 3 July 2014
3. Horan WP, Blanchard JJ (2003). "Emotional responses to psychosocial stress in schizophrenia: the role of individual differences in affective traits and coping". Schizophrenia Research 60 (2–3): 271–83.
4. Jauhar S, McKenna PJ, Radua J, et al. (2014). "Cognitive-behavioral therapy for the symptoms of schizophrenia: systematic review and meta-analysis with examination of potential bias".
5. Millar JK, Wilson-Annan JC, Anderson S, Christie S, Taylor MS, Semple CA, Devon RS, Clair DM, Muir WJ, Blackwood DH, Porteous DJ (2000). "Disruption of two novel genes by a translocation co-segregating with schizophrenia". Hum. Mol. Genet. 9 (9): 1415–23
6. Bradshaw, NJ; Porteous, DJ (2010-12-31). "DISC1-binding proteins in neural development, signaling and schizopherenia. Neuropharmacology. doi:10.1016 /j. neuropharm.2012
7. Millar JK, James R, Brandon NJ, Thomson PA (2005). "DISC1 and DISC2: discovering and dissecting molecular mechanisms underlying psychiatric illness.". Ann. Med. 36 (5): 367–78.
8. Miyoshi K, Asanuma M, Miyazaki I, et al. (2004). "DISC1 localizes to the centrosome by binding to kendrin.".Biochem. Biophys. Res. Commun. 317 (4): 1195–9.
9. Blackwood DH, Muir WJ (2004). "Clinical phenotypes associated with DISC1, a candidate gene for schizophrenia.". Neurotoxicity research 6 (1): 35–41.

CITATION OF THIS ARTICLE

Narmin M, Shima Rezaii A, Mohadeseh N,Khadijeh A, Venus H. Evaluation of DISC1 gene rs3738401 polymorphism in Iranian patients affected by Schizophrenia and normal individuals. Bull. Env. Pharmacol. Life Sci., Vol 4 [2] January 2015: 28-31