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ORIGINAL ARTICLE

Evaluation of DISC1 gene rs3738401 polymorphism in Iranian Multiple sclerosis (MS) patients affected by with type 2 Diabetes

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ABSTRACT

Multiple sclerosis (MS), also referred to as disseminated sclerosis or encephalomyelitis disseminate, is definitely an inflammatory disease in which the insulating covers of nerve cells in the brain and spinal cord are damaged. This damage disrupts the capability of elements of the nervous system to communicate, causing a wide variety of signs and symptoms, including physical, mental, and sometimes psychiatric problems.Type 2 diabetes referred to as adult-onset, is only a severe condition that affects the way in which your body metabolizes sugar (glucose), your body's important supply of energy. In this study, Evaluation of DISC1 gene rs3738401 polymorphism in Iranian Multiple sclerosis (MS) patients affected by with type 2 Diabetes was investigated. The present research was conducted including number of 70 Iranian Parkinson patients affected by type 2 Diabetes by employing ARMS-PCR process. To conclude, the information and statistics received from this study was analyzed by SPSS software. In summary, the end result of present study proves considerable relation between DISC1 rs3738401 polymorphism in Iranian Multiple sclerosis (MS) patients affected by with type 2 Diabetes. It could be a significant genetic predisposition factor.

Keywords: Parkinson, Diabetes, DISC1, rs3738401

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INTRODUCTION

Multiple sclerosis (MS), also recognized as disseminated sclerosis is absolutely an inflammatory illness in which the insulating covers of nerve cells in the brain and spinal cord are damaged. This harm disrupts the capability of areas of the nervous system to communicate, creating a broad selection of signs and symptoms, including physical, intellectual, and sometimes psychiatric troubles. MS takes various kinds, with new symptoms either occurring in isolated attacks (relapsing forms) or accumulating as time passes (progressive forms). (1) Between attacks, symptoms could vanish completely; however, permanent neurological problems frequently happen, especially as the disease advances.

There's no identified remedy for multiple sclerosis. Treatments attempt to enhance function after an attack and prevent new attacks. Medications used to deal with MS while modestly effective might have undesirable effects and be poorly tolerated. Lots of people pursue alternative treatments, despite deficiencies in evidence.(1)(2) The long-term outcome is difficult to predict, with good outcomes more often observed in women, those who develop the condition early in life, individuals with a relapsing

course, and people who initially experienced few attacks. Life expectancy is an average of 5 to 10 years lower than of an unaffected population. (3)
Type 2 diabetes is really a chronic disease in which individuals have problems regulating their blood sugar. People who suffer from diabetes have high blood sugar levels because their bodies produce enough insulin and aren't responsive to insulin or a combination of both. (4)
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].
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 [8].
The DISC1 gene is located at chromosome 1q42.1 and overlies with DISC2 open reading frame.(9) 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).
Schizophrenia, Bipolar disorder and schizoaffective disorder are usual psychiatric sickness with elevated heritability and changeable phenotypes.(10) 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 DISC1 [11]**.**
The present survey was done including a number of 70 in Iranian Multiple sclerosis (MS) patients affected by with type 2 Diabetes subjects by utilizing ARMS-PCR system. To conclude, the data received from this study were analyzed by SPSS software. In short, the result of current study shows considerable relationship between DISC1 gene rs3738401 polymorphism in Iranian Multiple sclerosis (MS) patients affected by with type 2 Diabetes. It could be a significant genetic predisposition aspect.

MATERIAL AND METHODS

This research was performed on 70 patients with Multiple sclerosis (MS) and 100 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.

PCR program used for DISC1 gene rs3738401 polymorphism:

cycle	temperature(Celsius)	Time
first	95	Minutes 7
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 (PH=8.3) , Ladder Were Used 50bp DNA Ladder (JenaBioscience) 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 Multiple sclerosis (MS).

RESULTS

We genotyped and analyzed 70 patients with Multiple sclerosis (MS) , and 100 healthy controls, 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 Multiple sclerosis (MS).

Table1: Genotype Table of DISC1 gene rs3738401 polymorphism:

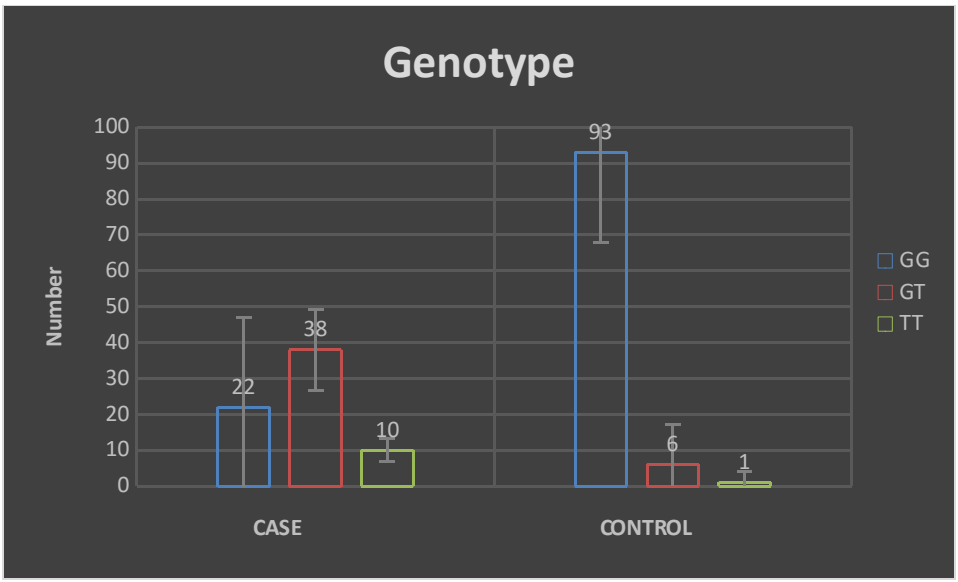
Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Genotype * Group	170	100.0%	0	.0%	170	100.0%

Genotype * Group Cross tabulation

Count

		Group		
		1	2	Total
Genotype	1	22	93	115
	2	38	6	44
	3	10	1	11
Total		70	100	170



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

Table2: ALLELE Table of DISC1 gene rs3738401 polymorphism:

Allele * Group Cross tabulation

Count

		Group		
		CASE	CONTROL	Total
Allele	G	82	192	274
	T	58	8	66
Total		140	200	340

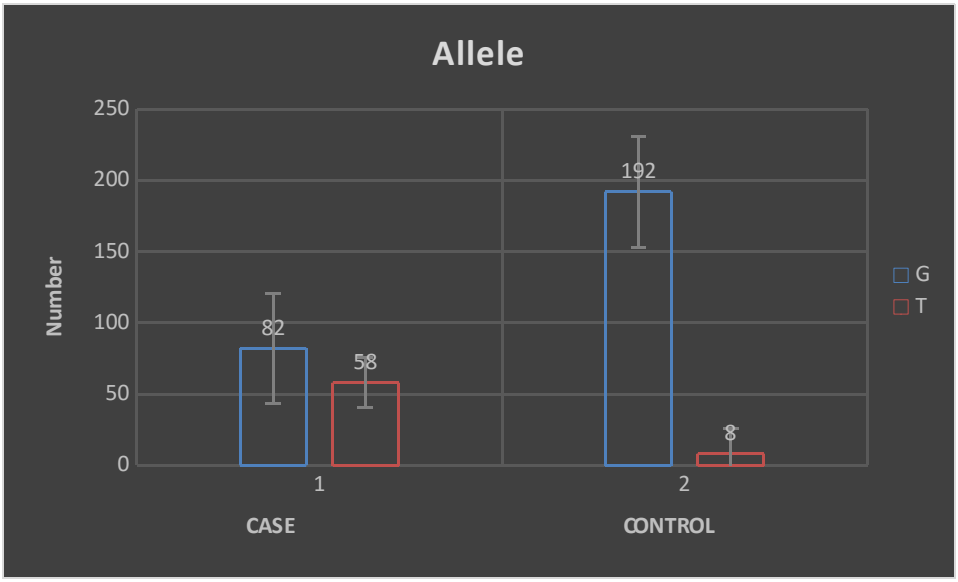


Table 2 showed that there were significantly correlation between DISC1 gene rs3738401 polymorphism and Multiple sclerosis (MS) . Therefore, DISC1 gene rs3738401 polymorphism may be a genetic predisposing factor for Multiple sclerosis (MS) in Iranian population.

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

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	71.401[a]	2	.000
Likelihood Ratio	76.330	2	.000
Linear-by-Linear Association	62.515	1	.000
N of Valid Cases	170		

a. 1 cells (16.7%) have expected count less than 5. The minimum expected count is 4.53.

DISCUSSION

The evidence uncovered in the article proves that DISC1 gene rs3738401 polymorphism plays a crucial role in Iranian Multiple sclerosis (MS) patients affected by with type 2 Diabetes. According to this, an improved frequency of the allele among patients with MS has been seen.

By analyzing a crowd of Iranian patients, it is found 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 Iranian Multiple sclerosis (MS) patients affected by with type 2 Diabetes. So, DISC1 gene rs3738401 polymorphism may be a genetic predisposing factor.

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