IMPLICATION OF THE RS5326 (G-94A) POLYMORPHISM OF THE DOPAMINE RECEPTOR GENE (DRD1) IN THE ONSET OF SCHIZOPHRENIA

I. Sdiri (1), N. Fekih-Mrissa (1), A. Oumaya (2), B. Nsiri (3)

(1) UR 17DN06, Service d'Hématologie, Hôpital Militaire Principal d'Instruction de Tunis, Tunisie

(2) Service de Psychiatrie, Hôpital Militaire Principal d'Instruction de Tunis, Tunisie

(3) Service d'Hématologie, Hôpital Militaire Principal d'Instruction de Tunis, Tunisie

Introduction

Schizophrenia is one of the most common and debilitating mental illnesses worldwide. It is a chronic psychotic disorder that affects emotional, cognitive, and social functioning. Several studies have indicated an association between genetic alterations in the dopamine D1 receptor gene (DRD1) and neuropsychiatric diseases.
These alterations can affect both the expression levels and the function of the D1 receptor, potentially contributing to the risk of developing schizophrenia by influencing the onset, progression, and response to treatment of the disorder.

Objective

The aim of our study is to determine the association between the rs5326 (G-94A) polymorphism in the 5'-untranslated region of the DRD1 gene and schizophrenia

Materials and methods

This study was carried out at the Molecular Biology Research Unit of the Hematology Laboratory at the Military Hospital of Tunis. It is a case-control study involving 60 patients with schizophrenia and 60 controls."

1. Genomic DNA extraction
2. DNA amplification « PCR »
3. Enzymatic digestion (RFLP)

The polymorphism rs5326 (G-94A) is a SNP located in the 5' untranslated region (5'-UTR) of the DRD1 gene

➔ To reveal the presence of the rs5326 polymorphism, the amplification product is subjected to enzymatic digestion using the restriction enzyme "FspBI". In case of mutation, there is a substitution of Guanine by Adenine at position 94 in the untranslated region of the DRD1 gene, which leads to the creation of a restriction site for,the "FspBI" enzyme.

➔ The amplification and digestion products are revealed by agarose gel electrophoresis.

➔ The distribution of genotypic and allelic frequencies was subsequently calculated and compared. Odds ratio and chi-square analyses were performed using Epi Info software

Results

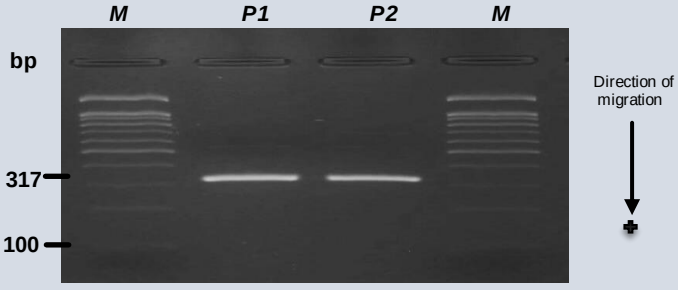

Fig1. Electrophoresis of PCR amplification products (rs5326 polymorphism), *M: 100bp molecular marker, P: subject (317 bp).*

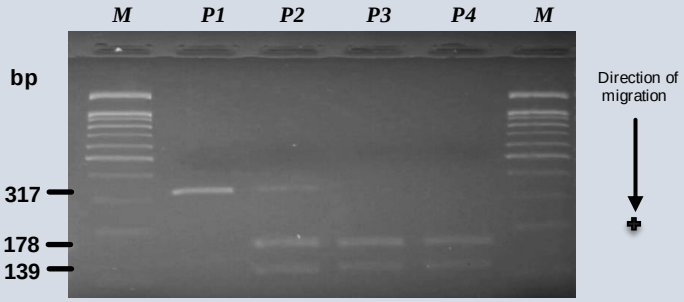

Fig2. Electrophoresis of digestion products (rs5326 polymorphism) M: 100bp molecular marker, P1: homozygous subject GG (317 bp), P2: heterozygous subject, GA (317 bp, 139 bp and 178 bp), P3 and P4: homozygous mutated subjects AA (139 bp and 178 bp)

Table1: Comparison of genotypic and allelic frequencies between patients and controls

Rs5326 (G-94A)	Patients		Controls	
	n	%	n	%
GG	43	71,66	50	83,33
GA	15	25	10	16,66
AA	2	3,33	0	0
G	101	84,16	110	91,66
A	19	15,83	10	8,33

Table2: Statistical analysis of genotypic and allelic frequencies between patients and controls

Rs5326 (G-94A)	χ^2	OR	[IC 95%]	P
GG	2.34	0,50	0,20-1,22	0,12
GA	1.26	1,66	0,68-4,08	0,26
AA	2.03	Non défini	Non défini	0,15
G	3,17	0,48	0,21-1,08	0,07
A	3,17	2,06	0,91-4,66	0,07

n: effectif, OR : Odds Ratio, IC : Intervalle de confiance, p : P Value (significative si p<0,05).

Our results show that the homozygous GG genotype is the most frequent in both groups, with a prevalence of 71.76% in patients vs. 83.33% in controls. The heterozygous GA genotype is more common in patients (25%) compared to controls (16.66%). The homozygous AA genotype is the least frequent in patients (3.33%) and absent in controls. Additionally, the G allele predominates in both groups, with a frequency of 84.16% in patients and 91.66% in controls. Statistical tests indicated that the differences between the two groups are not statistically significant (p-value > 0.05 and χ^2 value < 3.84),

Conclusion

Our results indicate that the rs5326 (G-94A) polymorphism in the DRD1 gene does not represent a risk factor for schizophrenia in our study population