Involvement of the 5-HTTLPR polymorphism of the serotonin transporter gene SLC6A4 in the onset of migraine

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INTRODUCTION

Migraine is a complex neurological disorder characterized by long-lasting unilateral headaches. The genetic component seems to play a crucial role in the susceptibility and manifestation of the disease, particularly genetic alterations that affect the functio ning of the serotonergic system and its components.

OBJECTIVE

The study aims to study a possible correlation between the 5-HTTLPR polymorphism of the serotonin transporter gene SLC6A4 in the onset of migraine

METHODS

The study is carried out within the molecular biology unit - Hematology Laboratory of the main military training hospital of Tunis

5-HTTLPR polymorphism

Insertion/deletion of 43 bp in the polymorphic 5-HTTLPR region located in the promoter sequence of the SLC6A4 gene, results in two allelic forms with different sizes and activities:

• **The long (L)** variant allele with the 43 bp insertion (512 bp) which increases the mRNA expression level and density of presynaptic 5-HTT (transporter) and therefore eliminates more serotonin from the synaptic cleft (maintain cerebral 5-HT homeostasis).

•**The short (S)** variant allele without 43 bp (469 bp) which produces lower levels of transporter mRNA, decreases its presynaptic density, and thereby reduces its activity.

Case-control study carried out on 60 migraine patients and 60 controls

1. • Genomic DNA extraction
2. • DNA amplification (PCR)
3. • Migration on agarose gel
4. • Calculate and compare the distribution of genotype and allele frequencies

RESULTS

The electrophoretic profile (fig) showed the presence of:

• A band of **469 bp** for the **homozygous SS** genotype
• A band of **512 bp** for the **homozygous LL** genotype
• Two bands **469 bp and 512 bp,** for individuals with the **heterozygous SL** genotype

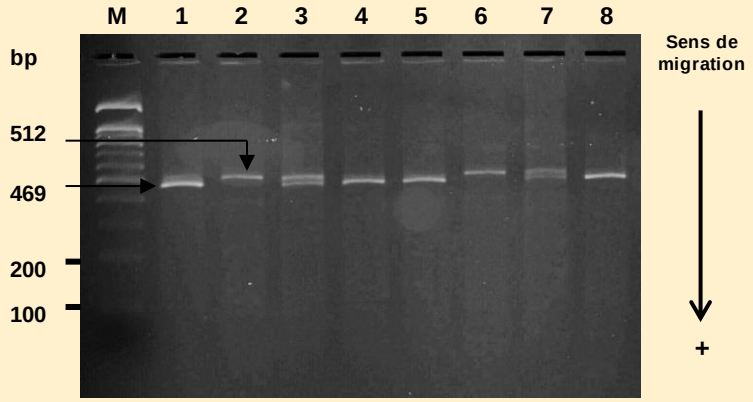

Fig: Electrophoretic profile of 5-HTTLPR polymorphism genotyping

M: Size marker (100 bp); 1, 4, 5, 8: Homozygous SS genotype (469 bp); 2, 6: Homozygous LL genotype (512 bp); 3, 7: Heterozygous SL genotype (469 bp + 512 bp)

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

	Patients %	Controls %	χ^2	OR	[CI 95%]	P
SS	53,33	58,33	0,30	0,81	[0,39-1,67]	0,58
LL	46,66	38,33	0,85	1,40	[0,68-2,91]	0,35
SL	0	3,33	2,03	0	indéfini	0.15
S	53,33	60	1,08	0,76	[0,45-1,27]	0,29
L	46,66	40	1,08	1,31	[0,78-2,18]	0,29

Chi-deux ($\chi 2$), *OR: Odds Ratio, CI: Confidence interval, p: P Value (significant if p<0.05).*

Analysis of genotype frequencies revealed that the homozygous SS genotype is common in both groups, with a frequency of 53.33% among patients and 58.33% among controls.
The LL genotype is more prevalent among migraine patients (46.66%) compared to controls (38.33%). Conversely, the heterozygous SL genotype is the least common in both groups (absent in migraine patients and very rarely present 3.33% in the control group)

Examination of allele frequencies indicated that the S allele is significantly more frequent in the control group (60%), while the L allele is more prevalent in migraine patients (48%).

The study of genotypic and allelic frequencies as well as the application of different statistical tests showed a statistically non-significant association between the 5-HTTLPR polymorphism and migraine with a p-value>0.05 and a $\chi 2$ value<3.84.

CONCLUSION

The molecular study of the SLC6A4 gene of the serotonin transporter, showed a statistically insignificant correlation for the polymorphisms, 5-HTTLPR, so it does not represent a risk factor for migraine.