

GENETIC CLUES IN NEUROINFLAMMATION: EXPLORING *NFKB1* AND *CCL2* VARIANTS IN ALS

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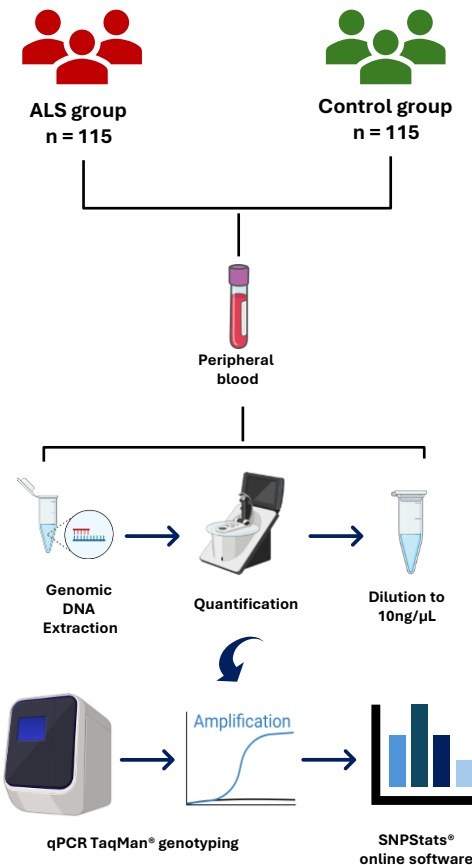
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INTRODUCTION

Amyotrophic Lateral Sclerosis (ALS) is a rare, progressive, and fatal neurodegenerative disease that affects motor neurons, leading to muscle weakness and atrophy. Although its etiology is not yet fully understood, factors such as glutamatergic excitotoxicity, genetic alterations, and neuroinflammatory processes have been implicated in its pathogenesis. Genes involved in the inflammatory response are being investigated for their potential contributions to the progression of neurotoxicity. This study aimed to evaluate the association of the rs3774959 (*NFKB1*) and rs4586 (*CCL2*) variants with susceptibility to ALS, considering their roles in the context of neuroinflammation.

METHODOLOGY



RESULTS AND DISCUSSION

Table 1. Association analysis between the rs3774959 polymorphism in the *NFKB1* gene and susceptibility to ALS.

Models	Genotypes	Case (115)	Controls (115)	OR (CI 95%)	p-value	AIC ^a	BIC ^a
Codominant	G/G	52 (45.2%)	43 (37.4%)	1.00			
	A/G	50 (43.5%)	59 (51.3%)	1.43 (0.82-2.48)	0.45	323.2	333.6
	A/A	13 (11.3%)	13 (11.3%)	1.21 (0.51-2.88)			
Dominant	G/G	52 (45.2%)	43 (37.4%)	1.00			
	A/G-A/A	63 (54.8%)	72 (62.6%)	1.38 (0.82-2.34)	0.23	321.4	328.3
	A/A	13 (11.3%)	13 (11.3%)	1.00 (0.44-2.26)	1	322.8	329.7
Recessive	A/A	13 (11.3%)	13 (11.3%)	1.00			
	G/G-A/A	65 (56.5%)	56 (48.7%)	1.00			
	A/G	50 (43.5%)	59 (51.3%)	1.37 (0.81-2.30)	0.23	321.4	328.3
Log-additive	---	---	---	1.20 (0.81-1.77)	0.37	322	328.9
Alleles							
	G	154 (67%)	145 (63%)				
	A	76 (33%)	85 (37%)		0.3059 ^a		

a Fisher's exact test; b Logistic regression; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion.

Table 2. Association analysis between the rs4586 polymorphism in the *CCL2* gene and susceptibility to ALS.

Models	Genotypes	Case (115)	Controls (115)	OR (CI 95%)	p-value	AIC ^a	BIC ^a
Codominant	C/C	25 (21.7%)	31 (27%)	1.00			
	C/T	56 (48.7%)	64 (55.6%)	0.92 (0.49-1.74)	0.088	320	330.3
	T/T	34 (29.6%)	20 (17.4%)	0.47 (0.22-1.02)			
Dominant	C/C	25 (21.7%)	31 (27%)	1.00			
	C/T-T/T	90 (78.3%)	84 (73%)	0.75 (0.41-1.38)	0.36	322	328.9
	C/T-C/T	81 (70.4%)	95 (82.6%)	1.00			
Recessive	T/T	34 (29.6%)	20 (17.4%)	0.50 (0.27-0.94)	0.029	318.1	324.9
	C/C-T/T	59 (51.3%)	51 (44.4%)	1.00			
	C/T	56 (48.7%)	64 (55.6%)	1.32 (0.79-2.22)	0.29	321.7	328.6
Log-additive	---	---	---	0.69 (0.47-1.01)	0.056	319.2	326.1
Alleles							
	C	106 (46%)	126 (55%)				
	T	124 (54%)	104 (45%)		0.078 ^a		

a Fisher's exact test; b Logistic regression; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion.

The rs3774959 variant in the *NFKB1* gene was not significantly associated with ALS under any of the inheritance models evaluated. In contrast, the rs4586 variant in the *CCL2* gene, under the recessive model, demonstrated a potential protective effect of the T allele, suggesting that individuals with the T/T genotype may have a reduced risk of developing ALS (OR = 0.50; 95% CI = 0.27–0.94; p = 0.029). This finding may be related to modulation of the inflammatory response mediated by the MCP-1 protein, as this variant introduces a premature stop codon.

CONCLUSION

This is the first study to investigate the association of these specific variants with ALS in the Brazilian population. The results reinforce the relevance of the inflammatory pathway in ALS pathophysiology and highlight the potential of these variants as genetic markers in precision medicine strategies, contributing to the development of population-tailored genetic screening panels.

REFERENCES



References



Curriculum Lattes

SUPPORT

