MONOCYTE CHEMOATTRACTANT PROTEIN-1 -2518A/G GENE POLYMORPHISM IS ASSOCIATED WITH SCHIZOPHRENIA IN ARMENIAN POPULATION

Zakharyan R[1,2], Khoyetsyan A[1], Chavushyan A[1], Navratilova Z[2], Arakelyan A[1], Boyajyan A[1], Mrazek F[2], Petrek M[2]

1 Laboratory of Macromolecular Complexes, Institute of Molecular Biology, National Academy of Sciences of Armenia,
2 Laboratory of Immunogenomics and Proteomics, Dept of Immunology, Medical Faculty of Palacky University, Olomouc, Czech Republic.

Introduction

Schizophrenia is a severe multifactorial mental disorder with unidentified etiology.

Alterations in the immune system play an important role in **schizophrenia pathogenesis**, nevertheless the molecular mechanisms of detected changes are not clear.

Monocyte chemoattractant protein-1 (MCP-1, CCL2) is a chemokine associated with several autoimmune and neuroinflammatory diseases.

Epidemiological studies as well as experimental findings suggest the **genetic component for schizophrenia.**

Rationale and Aim

Functional *MCP-1* gene variants may be considered as important **candidates** for **schizophrenia susceptibility** and clinical course.

The potential role of the ***MCP-1*** gene promoter **-2518A/G (rs1024611)** SNP in clinical heterogeneity and resistance to antipsychotic treatment in schizophrenia was shown (1,2).

The aim of this study was to evaluate the association of *MCP-1* functional variant *-2518A/G* with schizophrenia in Armenians.

(1) Pae et al., Psychiatr Genet 2004,14(2):65-7.
(2) Mundo et al., Am J Med Genet B Neuropsychiatr Genet. 2005, 132B(1):1-4.

Subjects and Methods

1) **Study population**

Patients with paranoid schizophrenia: N = 103

All patients were diagnosed as paranoid schizophrenics (F20.0) according to the international classification of mental diseases, 10th revision (ICD-10) by two independent experienced psychiatrists.

Control population: N = 105

Healthy volunteers without familial history of schizophrenia.

All individuals enrolled in this study were unrelated Armenians.

2) **Methods**

Genetic analysis

Genotyping for *MCP-1* -2518A/G SNP was performed using polymerase chain reaction with sequence specific primers (PCR-SSP).

Statistical analysis & power

The distribution of genotypes for *MCP-1* -2518A/G SNP was tested for compliance to the Hardy-Weinberg (H-W) equilibrium. The significance of differences in allelic and phenotype frequencies in patients and control subjects was determined by Pearson's Chi-square test.

Statistical power of the present study to detect the difference in the carriage of the *MCP-1* -2518*G allele between the patients and healthy controls for the odds ratio 2 reached 96.9%.

Results

The distribution of *MCP-1* -2518 genotypes complied to the Hardy-Weinberg expectations in both patients with schizophrenia and control subjects (**Table 1**).

The frequency of ***MCP-1* -2518*G** allele was significantly **higher in schizophrenic patients** (35%) **as compared to controls** (23%, *p*=0.009, OR=1.77, 95% CI: 1.1-2.04; **Fig. 1**).

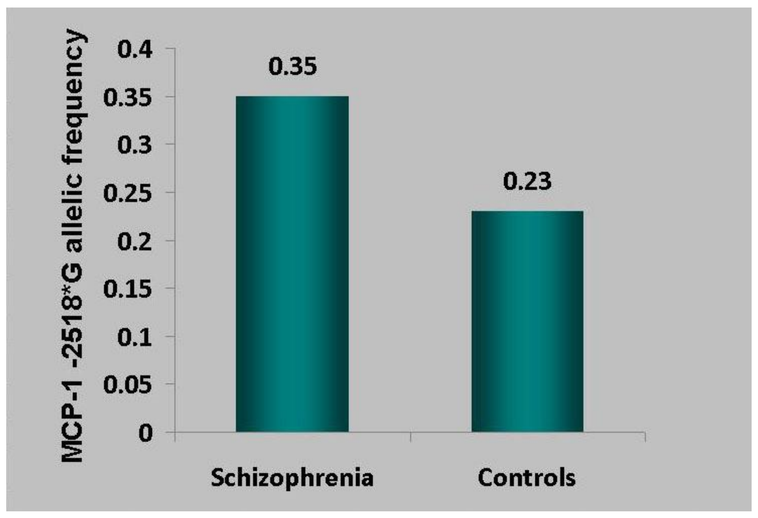
Furthermore, the ***MCP-1* -2518*G carriers were overrepresented in patients** (60%) **as compared to controls** (40%), *p*=0.003, OR=2.27, 95% CI: 1.13-2.01, **Fig. 2**).

Table 1: *MCP-1* -2518A/G genotypes and minor allele carriage rate in schizophrenia patients (SCZ) and healthy controls.

MCP-1 -2518	Schizophrenia	Control	*p*-value
Genotype AA	41 (0.40)	63 (0.60)	
Genotype AG	52 (0.50)	35 (0.33)	
Genotype GG	10 (0.10)	7 (0.07)	
Allele A	134 (0.65)	161 (0.77)	
Allele G	72 (0.35)	49 (0.23)	0.009[a]
Carriage G	62 (0.60)	42 (0.40)	0.003[b]

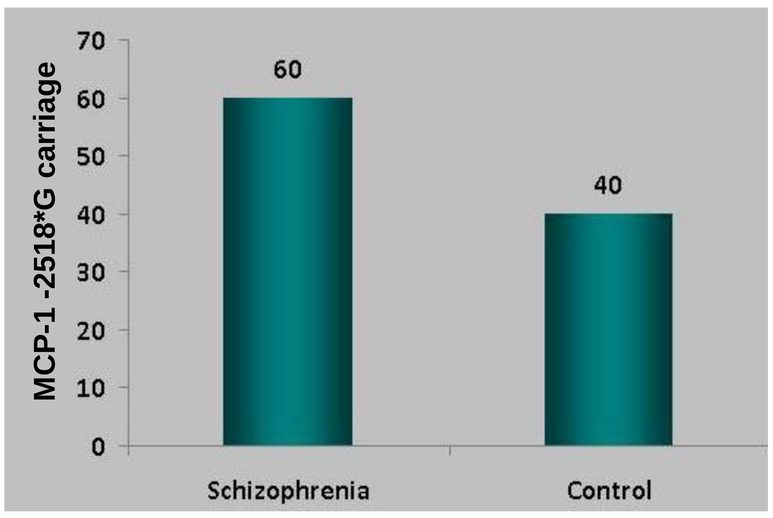
[a] *p*-value for comparison of G allele frequency between SCZ and controls;
[b] *p*-value for comparison of G allele carriage between SCZ and controls.

Figure 1: Comparison of *MCP-1* -2518*G allele frequency in schizophrenic patients and controls



Schizophrenia *versus* Controls:
p=0.009; odds ratio = 1.77; 95%CI = 1.1-2.04

Figure 2: Comparison of *MCP-1* -2518*G allele carriers in schizophrenic patients and controls



Schizophrenia *versus* Controls:
p=0.003; odds ratio= 2.27, 95% CI: 1.13-2.01

Conclusions

Our data suggest that *MCP-1* -2518*G allele or a variant in linkage disequilibrium might increase the risk for schizophrenia in Armenian population.

The association of studied *MCP-1* polymorphism with schizophrenia might be related to the alterations in inflammatory response.

Mechanisms by which this *MCP-1* variant implicates in the pathogenesis of schizophrenia remains to be clarified in further studies.

Because this is the first study indicating that *MCP-1* -2518A/G polymorphism is associated with schizophrenia susceptibility, it should be independently replicated.

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