Depression symptoms in Multiple Sclerosis patients – the role of IL1B

Andrea Bettencourt1,2, Bárbara Leal1,2, Marta Ferreira1, Cláudia Carvalho1,2, Inês Moreira1, Ernestina Santos1, Paulo Pinho e Costa1,2, Berta Silva1,2, Sara Cavaco1, Ana Martins da Silva1,2


Introduction

Neuropsychiatric symptoms, including depression, are relatively common in chronic autoimmune diseases such as Multiple Sclerosis (MS) [1, 2, 3]. It is still unclear whether depressed mood in MS is reactive to the disease (i.e., a secondary response to a chronic and unpredictable illness) or a manifestation of the neurobiological changes engendered by the disease itself. In recent years, several studies have demonstrated an imbalance in pro-inflammatory cytokine levels, such as IL-1β, in depressed individuals. Additionally, the rs16944 polymorphism, which predisposes to the production of higher IL-1β levels, has been associated with the development of both autoimmune diseases and depression.

Aims: To contribute to a better understanding of depression in MS, studying the association between rs16944 polymorphism and development of depression symptoms in MS patients.

Subjects and methods

A total of 156 MS patients and 217 ethnically-matched controls were studied (Table 1). MS patients underwent a full neurological examination and answered the Portuguese Hospital Anxiety and Depression Scale (HADS). DNA was extracted from peripheral blood using a salting out procedure. Rs16944 genotyping was performed using a pre-designed TaqMan allelic discrimination assay. Differences in frequencies were evaluated using Chi-Square test or Fisher’s exact test (when appropriate). Analyses were done with SPSS v.20 software and significant levels were set at p<0.05.

Results

No significant association was observed between rs16944 polymorphism and MS susceptibility.

Fourteen (8.8%) MS patients had pathological depression defined by HADS ≥11. Rs16944 TT frequency is higher in MS patients with HADS≥11 compared to MS patients with HADS<11.

Conclusions

The study results demonstrate that the rs16944 TT genotype is a susceptibility factor for the development of depression symptoms in MS patients. Even though this is the first study to explore such association in a MS cohort (to the best of our knowledge), similar results have been found for other chronic pathologies [4, 5, 6]. These findings suggest that a deregulation of the inflammatory reaction may contribute to the development of depression.

The rs16944 TT genotype has been described as an enhancer of IL-1β production. IL-1β overexpression may interfere with SNC functioning, particularly regarding to serotonergic neurotransmission, HPA system, and hippocampal neurogenesis (Figure 3). These mechanisms are putatively involved in the pathophysiology of depression.

References:


Figures:

Figure 1 - rs16944 genotypic frequencies in control population and MS patients.

Figure 2 - rs16944 genotypic frequencies in patients with and without depression symptoms.

Figure 3 - Pro-inflammatory cytokines and SNC functioning in depression development.