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Short Communication

Association Study of Interferon-γ and Interleukin 10 Gene Polymorphisms in Alzheimer Disease

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Introduction

Imbalanced inflammatory processes are clearly identified as major contributing factors in the progression of several neurodegenerative diseases affecting the elderly, including Alzheimer's Disease (AD). In AD, the inflammatory response is primarily localized in the vicinity of amyloid plaques. Environmental factors, combined with inherent genetic predispositions, appear to trigger these inflammatory responses, leading to an uncontrolled production of proinflammatory cytokines, including IFN-G, Tumor Necrosis Factor (TNF-α), interleukin (IL)-1β, and IL-6. This excessive and uncontrolled production ultimately leads to alterations in neuronal communication, behavior, and disease-related pathogenesis [1]. On the other hand, anti-inflammatory agents such as IL10 might play a protective role, combating the progression of neuronal degeneration. Therefore, only a limited number of studies have explored the association of the IL10 promoter and IFNG gene polymorphisms with dementia, and even fewer have investigated their association with AD. In this study, we aim to confirm these hypotheses using a sample of patients who have already been genotyped for Apolipoprotein E (ApoE), ApoA1, and Vascular Endothelial Growth Factor (VEGF).

Patients and Methods

This was a case-control study involving 243 adult Tunisian patients selected from the Neurology service of Sahloul University Hospital (Sousse, Tunisia). The group of probable AD patients comprised 93 patients (49 females and 44 males; mean age 73±0.87 years, n=93) diagnosed based on the criteria of the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA). The control group consisted of 150 Tunisians subjects (79 females and 71 males; mean age 71±1.78 years), with unknown personal or family history of dementia. DNA extracted from AD groups and control was performed using the Promega kit on peripheral blood samples. IL10 genotype and IFNG polymorphism were assessed in 243 subjects using Polymerase Chain Reaction (PCR) and Restriction Fragment Length Polymorphism (RFLP) methods, as described previously.

Results and Discussion

Our data revealed that the -1082G/A polymorphism of the IL10 gene cannot be considered as a genetic susceptibility factor for Alzheimer's disease (p=0.24), as we did not observe that a statistical difference in the genetic distribution of the G/A genotype and the A allele (p=0.6). German and Italian studies have also reported this association [2-4], although other studies have not been able to replicate these results [5-7], and it has been suggested that the role of the IL10 gene in AD susceptibility may be limited to certain populations [8-10], which indicates the need for further studies.

In the case of the IFNG polymorphism, we did not find statistically significant differences in allele frequencies when comparing the AD and the control groups ($\chi 2=3.492$; p=0.24 for alleles). The distribution of the IFNG genotypes was found to differ significantly from that the control group ($\chi 2 =26$, df=2 p=0.001). OR for the IFNG AA homozygous subjects was 1.94 (95% CI= 1.09-3.47), p= 0.016. With regard to IFNG polymorphism, previous studies showed that the +874 AA genotype of the INFG gene is associated with higher risk of AD compared with the wild homozygous genotype (OR=2.22). However, this disagrees with the Feher [11], which showed that the A/A genoype for IFNG was not significantly associated with AD and by others who failed to demonstrate any

association between the +874 A/T polymorphism and AD [12]. The controversial results among different studies may also reflect the difference in distribution of IFNG in different ethnic populations and/or a distinct linkage of IFNG with a nearby AD susceptibility gene, yet to be identified, in different populations [13].

Conclusion

In summary, our findings confirm the hypothesis that the IFNG+874 T/A polymorphism is associated with late-onset AD. However, the IL-10-1082 A/G polymorphism does not increase the risk of developing AD. This finding could be an important target for therapeutic strategies aimed at limiting the inflammatory response involved in the development of the disease. Furtssher studies addressing other single nucleotide polymorphisms and variants of the IL10 gene are required.

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Conflict of Interest

None.

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