

Association between IL-10-1082 gene polymorphism and risk of Alzheimer's disease

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Abstract: Objective: To explore the association between interleukin-10 (IL-10)-1082 gene polymorphism and the occurrence of Alzheimer's disease (AD).

Methods: A total of 160 AD patients and 280 healthy controls were selected from January 2023 to December 2024. Clinical and epidemiological data were collected. PCR-RFLP was applied to compare the distributions of genotypes and alleles between two groups.

Results: Regarding IL-10-1082 gene polymorphism, the frequencies of AA and A were significantly higher in AD group compared with those in control group ($P < 0.05$).

Conclusion: In conclusion, the IL-10-1082G/A gene polymorphism is an independent risk factor for the development of AD and can be used as a genetic marker to identify individuals at increased risk of developing AD.

Keywords: Alzheimer's disease; Genetic association; Gene polymorphism; IL-10.

Introduction

Alzheimer's Disease (AD), commonly known as senile dementia, refers to a specific onset process of age-related cognitive and functional decline, eventually leading to death^[1]. AD is a neurodegenerative disease characterized by damage to brain regions responsible for controlling memory and other cognitive functions^[2]. AD patients not only have impaired abilities in learning, reasoning, communication and daily activities, but also are often accompanied by personality and behavior changes, which seriously affect the quality of life of patients^[3]. With the increasing aging of the population, AD has become a global public health problem of great concern. According to the World AD Report 2021, it is estimated that the number of AD patients in the world will reach 78 million in 2030, of which 20.75 million will be in China^[4]. According to the data of AD report in China, the number of AD patients and other dementias in China is 13,143,950, of which AD accounts for 60% ~ 80%^[5], accounting for about 25.5% of the global number. China's AD prevalence and mortality are higher than the global average. Therefore, understanding the related mechanisms of AD is of great significance for ensuring the quality of life of patients and exploring early scientific and effective intervention and treatment methods.

The neuropathological features of AD are changes in amyloid - beta ($A\beta$) plaque formation and hyperphosphorylation of tau protein associated with neurofibrillary tangles. In recent years, with the deepening of research, scholars have proposed a new theory that the immune inflammatory response mechanism is another major pathophysiological factor related to the pathogenesis of AD, which involves the disorders of the blood-brain barrier, neurons, microglia, astrocytes and various cytokines. Activated microglia and astrocyte clusters at the site of neuritis plaques release multiple inflammatory mediators, including pro-inflammatory and anti-inflammatory cytokines, which play a key role in the development and progression of AD.

Among them, interleukin-10 (IL-10), as an anti-inflammatory mediator, has been shown to be one of the major cytokines related to the occurrence of AD. AD is a genetic disease, and some studies have speculated that IL-10 gene polymorphism is an important risk factor for its onset. Due to the difference in genotype distribution of IL-10 polymorphism between Caucasians and Asians, there is a lack of clinical reports on the correlation between IL-10 1082 gene polymorphism and AD in Asian populations, and the relationship between risk factors of AD and IL-10 1082 gene polymorphism has not been fully studied. Therefore, the purpose of this study was to investigate the gene polymorphism for AD in Eastern population of China.

Materials and methods

Research subjects

Newly diagnosed AD patients from January 2023 to December 2024 were included, and healthy controls with normal cognitive function matched by age, sex and education level were included during the same period. All subjects in this study signed informed consent and were approved by the Ethics Committee.

Inclusion and exclusion criteria

AD enrollment criteria: According to the National Institute on Aging and the Alzheimer's Association^[6], the diagnostic criteria are revised as follows: (1) meet the diagnostic criteria for AD; (2) MMSE score: illiteracy is lower than 17 points, primary school less than 20 points, secondary school and above education less than 23 points; (3) CDR is 1 ~ 2 points; (4) Hachinski score ≤ 4 points. Exclusion criteria: (1) Patients with high white matter signal Fazakes grade $\geq II$; (2) Have a history of severe anxiety, depression, physical disorders, mental illness; (3) Cognitive impairment caused by stroke, Parkinson's disease, lewy body dementia and other neurological diseases; (4) Patients with liver and kidney diseases, epilepsy, thyroid diseases, rheumatism and immune diseases, digestive diseases, and malignant tumors; (5) Patients who have taken folic acid or other B vitamins in the past 1 month, and have a history of taking drugs such as intelligence promoting drugs, methotrexate, isoniazid, carbamazepine, and levodopa. (6) People with

metal implants such as cochlear implants and cardiac pacemakers; (7) Patients with contraindicated or intolerant head MRI examination; (8) those who have not signed the informed consent

Gene Polymorphism Analysis

Approximately 3 mL of venous blood was collected in the morning and placed in an EDTA anticoagulant tube for DNA extraction by applying Kit (Thermo Fisher Company, USA). Amplification was performed using the PCR-restriction fragment length polymorphism (PCR-RFLP) method, following protocols from previous literature. Gene polymorphism analysis was carried out using ABI3730XL and GeneMapper 4.1, with sequencing for further verification.

Statistical analysis

The degree of correlation was statistically determined using odds ratios (ORs) and 95% confidence intervals (CIs). Statistical analysis for the experimental portion was performed using SPSS 19.0, employing the t-test for measurement data and the χ^2 test for categorical data. A P-value <0.05 was considered statistically significant.

Results

General Characteristics of Study Subjects

Table 1 outlines crucial information about the study subjects. There were no significant differences between the two groups in terms of age, sex, alcohol consumption or diabetes (P>0.05).

Table 1 Participates characteristics of AD group and control group

characteristics	AD group (N=160)	control group (N=280)	p
Age	68.8±7.1	67.6±6.8	0.08
Men	115(71.9%)	192(68.6%)	0.47
BMI	24.8±1.8	24.6±1.8	0.26
Smokers	44(27.5%)	80(28.5%)	0.33
Drinking history	33(20.6%)	55(19.6%)	0.73
diabetes mellitus	32(20.0%)	52(18.6%)	0.83
hypertension	34(21.3%)	57(20.4%)	0.70

AD, Alzheimer's disease; BMI, body mass index.

Genotyping and Allele Distribution of IL-10 Polymorphism

Analysis of the IL-10 gene polymorphism revealed three genotypes: GG, GA, and AA. Significant associations were observed for both the AA genotype and the A allele (all P<0.05), as detailed in **Table 2**. This underscores the potential significance of IL-10 polymorphism in the context of genetic susceptibility to AD.

Table 2. IL-10 genotype and allele frequency for AD group and control group

IL-10 loci	control group (N=280)		AD group (N=160)		OR(95%CI) a	Pa
	n	Percentage(%)	n	Percentage(%)		
GG	102	36.4	30	18.8	1.00REF	
GA	114	40.7	82	51.2	2.45(1.49-4.02)	<0.001
AA	64	22.9	48	30.0	2.55(1.47-4.43)	<0.001
G	318	56.8	142	44.4	1.00REF	
A	242	43.2	178	55.6	1.65(1.25-2.17)	<0.001

AD, Alzheimer's disease; OR, odds ratio; CI, confidential index; a Adjusted for by logistic regression model.

Discussion

AD is a central neurodegenerative disease that occurs in old age and early old age, characterized by progressive cognitive decline and mental and behavioral impairment, and is the main cause of dementia, and is rapidly becoming one of the deadliest and most burdensome diseases for patients, family members and society in this century. According to the Alzheimer's Association International's "World Alzheimer's Disease Report 2018," about 50 million people worldwide have AD. In recent years, with the increase of human longevity and aging, the prevalence of AD is rising, and unless breakthroughs are made in the prevention, mitigation or treatment of AD, the number of AD patients is expected to increase to more than 150 million by 2050. In China alone, the 2020 Epidemiological survey of Cognitive Disorders shows that there are 15.07 million dementia patients in China aged 60 and above, including nearly 10 million AD patients. The two core pathological features of AD include the deposition of extracellular amyloid plaques and the formation of intracellular neurofibrillary tangles.

Our results suggest that people with the AA genotype have a higher risk of developing AD. Specifically, people with the AA genotype were 2.55 times more likely to develop AD than those with the GG genotype. People with the A allele were 1.65 times more likely to develop AD than those with the GG allele. Our results are different from previous studies, to be precise, from both European and Chinese populations. But we don't think this result is surprising, because genetic research, especially the study of genetic polymorphism, is subject to many and complex factors. Different countries, regions, races, geography, climate, and environments can all bring about different effects, which can produce different results. This point has been confirmed by a large amount of literature and is widely recognized by the medical community^[7-16].

The current study inevitably has some inherent defects. First, the sample size is not very large, and second, the meta-analysis cannot be carried out simultaneously. Meta-analysis is a hot topic in current research, and its role in promoting biomedicine is increasing day by day^[17-25].

In conclusion, the IL-10-1082G/A gene polymorphism is an independent risk factor for the development of AD and can be used as a genetic marker to identify individuals at increased risk of developing AD.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

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Author contributions

Hongwei Zhao conceived study design and conceived the content concept; Jing Wang and Yuexiao Zou performed the data collection, extraction and analyzed the data. Yun He, Junqi Zhao and Shixue Wang interpreted and reviewed the data and drafts. Hongwei Zhao reviewed the final draft. All authors were involved in literature search, writing the paper and had final approval of the submitted and published versions.

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Disclosure

The authors declare that they have no competing interests.

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