

양극성 장애 환자에서 Apo-1/Fas Promoter 유전자 다형성*

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Association of a Polymorphism in the Promoter Region of Apo-1/Fas Gene with Bipolar Disorder*

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ABSTRACT

Objective : Recently, many experimental evidences have been reported that psychiatric diseases are closely related with neurodevelopmental abnormalities and this can be properly explained by apoptosis. It is known that Apo - 1/Fas is one of the genes in charge of apoptosis related with neurodevelopmental abnormalities. In this study, the association between bipolar disorder and functional polymorphism in Apo - 1/Fas promoter gene has been investigated.

Method : For 81 bipolar disorder patients and 217 healthy control subjects, Mval restriction fragment length polymorphism(RFLP) of Apo - 1/Fas promoter gene was analyzed after polymerase chain reaction(PCR) amplification.

Result : There was a statistical significant difference in genotypic distribution($\chi^2=16.656$, $df=2$, $p=0.0002$) and allelic frequencies($\chi^2=14.225$, $df=1$, $p=0.0002$) between bipolar disorder patients and healthy control subjects.

Conclusion : Our results suggest an association between functional polymorphism in Apo - 1/Fas promoter gene and bipolar disorder and provide the important genetic information related with the pathogenesis of the disease. Further studies employing larger samples are required to clarify the present results.

KEY WORDS : Apo - 1/Fas gene · Bipolar disorder.

서 론

가

(01 - PJ8 - PG6 - 01NE01 - 0003).

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가 33 (41%) 34.6 ± 8.7

1)

2) 217 가 105

가 (48.4%), 가 112 (51.6%) 41.8 ±

3) 4) 5) 11.5

2. 연구방법

1) DNA 분리

2ml

EDTA가 tube 24

DNA 가 - 20

DNA Isolation Kit(Roche, Mannheim, Germany) 2ml

6ml 가 10

tube isopropranolol 650ul

가 (apoptosis) 8)9) 10 1.5ml tube

Apo - 1/Fas(CD95) 468ul 10

70% ethanol 900ul

DNA 10

Apo - 1/Fas(CD95) TE 200ul

promotor 가 ,¹⁰⁾¹¹⁾ 5 flanking (polymerase chain reaction, PCR)

가 .¹²⁾ - 20

2) DNA의 중합효소 연쇄반응(PCR)

Apo - 1/Fas(CD95) Apo - 1/Fas promotor

Apo - 1/Fas promoter (primer) Huang¹³⁾

방 법

1. 연구대상

2

DSM - (American Psychiatric Association, 1994)

81 가 48 (59%),

Sense : 5' - CTACCTAAGAGCTATCTACCGTTC - 3'

Antisense : 5' - GGCTGTCCATGTTGTG-GCTGC - 3'

DNA PCR 100ng/ul DNA 1ul 2.5mM dNTP 1ul, 10pmol primer 1ul, Taq polymerase(Neurotics, Daejeon, Korea) 0.2ul(1 unit), 10 PCR 3ul, 3 23.3ul 가 30ul Mas- ter cycler gradient(Ependorf, Hamburg, Germany)

94 5 , denatura-
 tion 95 30 , annealing 58 60 , ex-
 tension 72 60 40
 extension 72 7

PCR DNA (332bp) ethidium bro-
 mide가 1.5% agarose gel
 UV transilluminator

3) 유전자형의 판별

PCR DNA 7ul Mval(Ro-
 che, Indianapolis, IN) 0.15ul, 2ul, 3
 10.85ul 가 20ul
 37 14 ethi-
 dium bromide가 3% agarose gel 100V
 UV transilluminator

(1). -670 A G
 3가 ,
 Mval 233/99bp
 (A/A homozygote), 188/99/45bp

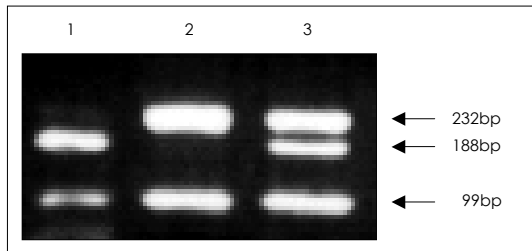


Fig. 1. Genotype analysis of Mval RFLP in Apo-1/Fas promoter region. 1 : GG homozygous genotype ; 2 : AA homozygous genotype ; 3 : A/G heterozygous genotype.

(G/G homozygote), 233/188/99/45bp
 (G/A heterozygote)

3. 통계 분석

Fas/Apo -
 1 promoter
 Analysis System(SAS) Statistic
 χ^2 - test
 , p<0.05

결 과

1. Apo-1/Fas 유전자의 유전자형과 대립유전자 발현율 및 빈도

Fas/Apo - 1 promo-
 ter (genotype frequency)
 (allele frequency) 1
 Mval RFLP A/A
 31(38.3%), G/G 16(19.7%), G/A 34(42.0%)
 A 96(59.26%), G 66
 (40.74%) Mval RFLP
 A/A 36(16.6%), G/G 71(32.7%), G/A
 110(50.7%) , A 182
 (44.25%), G 252(55.75%)

2. 양극성 장애 환자군과 대조군 사이의 유전자형과 대립유전자의 발현율 및 빈도의 비교

(χ^2 = 16.66, df = 2, p = 0.0002)

Table 1. Allele frequencies and genotype distribution for Apo-1/Fas polymorphism in Korean bipolar patients and control subjects

	Genotypes(%)			Allele frequency(%)	
	A/A	G/G	A/G	A	G
Controls(n=226)	36(16.60%)	71(32.70%)	110(50.70%)	182(44.25%)	252(55.75%)
Patients(n=81)	31(38.27%)	16(19.75%)	34(41.98%)	96(59.26%)	66(40.74%)
χ^2 value	16.656			14.225	
df	2			1	
p value	0.0002*			0.0002*	
Odd ratio				2.014	
(95% CI)				(1.395 - 2.906)	

* : statistical significance at the level of p<0.05

($\chi^2=14.2254$, $df=1$, $p=0.0002$)
 가 . odd ratio G 가 .¹³⁾²⁴⁾
 A odd ratio가 가
 2 (OR=2.014 가 .
 [1.395 - 2.906]).

고 찰

(cell - mediated immunity)

²⁵⁾

Apo - 1/Fas(CD95) 가 .
 가 .
 Apo - 1/Fas promoter .
 가 .
 Apo - 1/Fas ,
 (Alzheimer 's dise- 가
 ase) (Down syndrome)
 Apo - 1/Fas 가 .
¹⁴⁾¹⁵⁾ 가 .

(neurodegenerative disease)
 가 (neuro - plasticity)

¹⁶⁾¹⁷⁾

가 ,¹⁸⁾¹⁹⁾

(Huntington 's disease)
 (neurodegeneration) gliosis
²⁰⁾
 (cell loss) (atrophy) (neu-
 roprotective/neurotrophic)

결 론

81 217
 Apo - 1/Fas promo-
 ter Mval
 (restriction fragment length polymorphism, RFLP)

Mval RFLP

lit-
 hium 가 Bcl - 2 가
²¹⁾²²⁾
 , Apo - 1/Fas(CD95) tumor necrosis factor
 (TNF)

($\chi^2=16.656$, $df=2$, $p=0.0002$)
 ($\chi^2=14.225$, $df=1$, $p=0.0002$)

Apo - 1/Fas promoter 가

²³⁾

가

Apo - 1/Fas

중심 단어 : Apo - 1/Fas

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