

정신분열증환자와 도파민 D₁ 수용체 대립유전자 연합김정일* · 이민수*[†] ·곽동일*Association between the Alleles of the Dopamine D₁ Receptor and SchizophreniaJeong Il Kim, M.D.,* Min Soo Lee, M.D.,*[†] Dong Il Kwak*

ABSTRACT

The results regarding an association between the polymorphism sites in the dopamine D₁ receptor gene and schizophrenia compelled us to study the distribution of the polymorphism in Korean schizophrenia and controls. Eighty-eight schizophrenic patients and normal controls were examined by case-control study for distribution of the polymorphism of the dopamine D₁ receptor gene in Korean population to minimize the effect of racial differences in gene frequencies.

The frequencies of the B₁ and B₂ in schizophrenic patients were 0.11 and 9.89, respectively. And 0.10 and 0.90 in normal control. There was no significant differences in the frequencies in the allele B₁ and B₂ between schizophrenic patients and normal controls.

The author present here the evidence of a lack of allelic association between the polymorphism of the dopamine D₁ receptor gene and Korean schizophrenic patients. The assumption that the dopamine D₁ receptor gene has a genetic role in the development of schizophrenia was not supported by this case-control study.

KEY WORDS : Schizophrenia · Dopamine D₁ receptor · Allelic association.

서 론

가

가 ,

가

(ge-

nome)

(phenotype)

(linkage)

가

(polygenic

가

가 가

multiple threshold theory)

(Fara-

one Tsaung 1985),

(O'Rourke 1982),

(Tsaung

1982)

(penetrance)가

(Ba-

ron 1986),

가 가 가 ,

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[†] : , 136 - 705 5가 126 - 1) (02) 920 - 5354,) (02) 923 - 3507

(Amos 1991 ; Gelshon Goldin 1987).

가 ,

(allelic association) 가 uency) (prevalence) 가

가 가

dopamine D₁

receptor가

가 가 가

연구 대상 및 방법

1. 연구대상

1) 대상환자군

1992 3 1996 2

가

(Gerschon

DSM - III - R(APA 1987)

1994). 5가

가 가

20 57

가 가

5가

88 , 가 54 , 가 34

가

1.58 : 1 , 35.8 ± 7.9 (Table 1).

(Coon 1993 ;

2) 정상대조군

Jensen 1993 ; Gejman 1994 ; Jonsson 1993 ; Mac - ciardi 1994 ; Moises 1991 ; Nanko 1993 ; Sabate 1994 ; Seeman 1993 ; Shaikh 1994 ; Su 1993).

(polymerase chain reaction ;

PCR) 가 D₂, D₃, D₄

(1994 ;

1995 ; 1995)가

D₂(

88 , 가 54

1995) D₃(1995), D₄(

, 가 34 1.58 : 1 , 36.

1995)

0 ± 7.7 가

(Table 1).

D₂

D₁

2. 연구방법

(Seeman 1989),

D₁ (affinity) (high and low)

(candidate gene)

가

가 가 가

(Mamelak 1993). D₂

D₁

1) DNA의 정제

D₁

1.5ml 13,000rpm

(Ames 1996 ; Kaplan , pellet ACE shocking (NH₄Cl 8g, Na₂ ED -

1994).

Table 1. Demographic data

Diagnosis	No	Sex	Mean age±SD
Schizophrenics	88	54 M, 34 F	35.8±7.9
Control	88	54 M, 34 F	36.0±7.7

(allele) (genotype) D₁ (freq -

TAH₂O 1g, KH₂PO₄ 0.1g 1L) 500 μl
 3 2
 pellet 400 μl nucleic ly -
 sis buffer [Tris(pH8.0) 10mM, NaCl 400mM, EDTA 2mM]
 pellet 10% SDS 27 μl pr -
 oteinase K 10 μl 가 56 2
 (saturated) NaCl 135 μl 15
 . 13,000rpm 1
 2 DNA
 . DNA 70%
 100 μl

2) 중합효소 연쇄반응(polymerase chain reaction : PCR)을
 이용한 도파민 D₁ 수용체 유전자좌의 분석
 D₁ Cichon (1994)

(primer) Cichon (1994)

5' - ACTGACCCCTATTCCCTGCT - 3'

5' - AGCACAGACCAGCGTGTTTC - 3'

25 μl 35

template DNA	50ng
primer	25pmol
MgCl ₂	1.5mM
tris - Cl(pH8.3)	10mM
KCl	50mM
gelatin	0.1%(w/v)
dNTP	20 μM
Taq polymerase	1U

25 μl

94	5	1	94
30 , 50	30 , 72	30	35
	72	5	1

3) 증폭된 생성물의 분석

207bp (Ddel)

146bp+61bp B₁, 146bp+42bp+19bp

B₂ B₁ B₂

Ddel 10% PA -

GE gel ethidium bromide

(ultraviolet transilluminator) , pol -

aroid (polaroid film 667)

3) 통계분석방법

(Chi - square)

2 × 2 (contingency table) (continuity correction)

p < .05

(prevalence) (frequency)

Comings (1991)

연구 결과

가 (Table 1).

Table 2 (Table 2). D₁

PCR B₁B₁, B₁B₂, B₂B₂ 3
 가 DNA 88

B₁B₁ 3 , B₁B₂ 13 , B₂B₂ 72 85.2%,

14.8% , 88

B₁B₁ 1 , B₁B₂ 15 , B₂B₂ 72 83.0%,

17.0% . B₁

B₂ 18.2% , 96.6% ,

18.2% 98.9% .

B₁ B₂ 0.11 0.89,

0.10 0.90 (Table 2, 3, Fig. 1, 2).

Table 2. Genotype and allele frequencies of dopamine D1 receptor in schizophrenic patients and controls

Group	No	DRD ₁			Allele		Frequency of allele	
		B ₁ B ₁	B ₁ B ₂	B ₂ B ₂	B ₁	B ₂ (%)	B ₁	B ₂
SPR	88	3	13	72	16(18.2)	85(96.6)	0.11	0.89
Controls	88	1	15	72	16(18.2)	87(98.9)	0.10	0.90

= 1.14 df=2 non-significance SPR : Schizophrenics

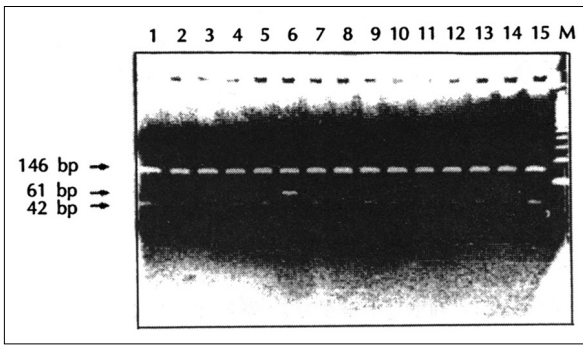


Fig. 1. PCR analysis of Dde I Restriction fragment length polymorphisms in Dopamine D₁ receptor alleles for schizophrenic patients.
 No. 1 : B₂B₂ homozygote. 2 : B₂B₂ homozygote. 3 : B₁B₂ heterozygote. 4 : B₂B₂ homozygote. 5 : B₂B₂ homozygote. 6 : B₁B₁ homozygote. 7 : B₂B₂ homozygote. 8 : B₁B₂ heterozygote. 9 : B₂B₂ homozygote. 10 : B₂B₂ homozygote. 11 : B₂B₂ homozygote. 12 : B₂B₂ homozygote. 13 : B₂B₂ homozygote. 14 : B₂B₂ homozygote. 15 : B₂B₂ homozygote. M : 100bp DNA size marker. PCR products were run on a 5% PAGE/0.5X TBE gel.

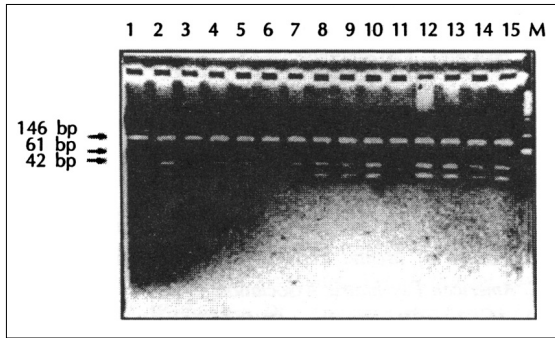


Fig. 2. PCR analysis of Dde I Restriction fragment length polymorphisms in dopamine D₁ receptor alleles for normal controls.
 No. 1 : B₂B₂ homozygote. 2 : B₂B₂ homozygote. 3 : B₂B₂ homozygote. 4 : B₁B₂ heterozygote. 5 : B₂B₂ homozygote. 6 : B₁B₂ heterozygote. 7 : B₂B₂ homozygote. 8 : B₂B₂ homozygote. 9 : B₂B₂ homozygote. 10 : B₂B₂ homozygote. 11 : B₂B₂ homozygote. 12 : B₂B₂ homozygote. 13 : B₂B₂ homozygote. 14 : B₂B₂ homozygote. 15 : B₂B₂ homozygote. M : 100bp DNA size marker. PCR products were run on a 5% PAGE/0.5X TBE gel.

고 찰

DNA (1994), (1995), (1995), (1995)
 가
 가
 3 , 5 , 11 , 18 , 19 , X 가
 가 가 가
 가 5 가 가
 5 Basset (1988) 가 5
 (trisomy)

(translocation) 가 . Sherrington (1988) (autosomaldominant) 가 (restriction fragment length polymorphism ; RFLP) (Kennedy 1989), (St Clair 1989), (Detera - Wadleigh 1989), (Diehl 1989), (McGuffin 1990) 가 5 Sherrington (1993) (microsatellite polymorphism) (1993) (1995) 3가 5 D5S39, D5S76 5 Dearry (1992), Sunahara (1990), Zhou (1990) D₁ 가 5 (5q35.1) (Grandy 1990 ; Liti 1991) 5 5가 D₁ D₂ 가 (Grandy 1990). D₁ 가 , adenylate cyclase D₂ 가 가 (Tsaung 1982), (Baron 1986), (Amos 1991 ; Gelson Goldin 1987) 가 가 (Davis 1991) 가 가 (Smeraldi Macciadi 1991 ; Sobell 1993). D₁

B_1 B_2
 Coming (1991)
 B_1
 B_1B_1 B_1B_2 , B_2 B_2B_2 B_1B_2
 가
 B_2 B_1 B_2 B_1
 5
 가
 D_1
 (Coon
 1993 ; Jensen 1993 ; Liu 1995).
 (Javitch Kaufman
 1991 ; Seeman 1993).
 가
 ga -
 mma aminobutyric acid ,
 가
 결론
 D_1
 88
 D_1
 B_1 B_2
 0.11 0.89, 0.10 0.90
 가
 D_1 가
 D_1 가
 D_1
 가
 중심 단어 : D_1

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