

정신분열병환자에서 만발성 운동장애와 5-HT₆ 수용체 유전자 다형성(267C/T)과의 관계

한상우*[†] · 김동현* · 전용호**

Association between Tardive Dyskinesia and 267C/T Polymorphism of 5-HT₆ Receptor Gene in Schizophrenia

Sang-Woo Han, M.D., Ph.D.,*[†] Dong-Hyeon Kim, M.D.,* Yong-Ho Jun, M.D.**

ABSTRACT

Objectives : Tardive dyskinesia(TD) is a serious side effect associated with long - term antipsychotic treatments. Some candidate genetic polymorphisms were reported to be associated with TD and possible involvement of serotonergic receptors in the pathophysiology of TD has been suggested. In the present study, we investigated the association between 5 - HT₆ receptor gene polymorphism and TD with schizophrenia.

Methods : To investigate the relationship between 5 - HT₆ receptor gene polymorphism and TD, 60 patients with TD were compared with 60 patients without TD. The 267C/T allele of 5 - HT₆ receptor gene was genotyped by means of polymerase chain reaction method. TD was evaluated using the Abnormal Involuntary Movement Scale(AIMS).

Results : The patients with the three 267C/T genotype showed no significant differences in age, gender, and duration of illness. No significant difference in genotype frequencies was observed between schizophrenic patients with and without TD. In addition, there was no difference in allele frequencies. Further analysis with an measure of AIMS scores showed that these scores were not significantly influenced by the 5 - HT₆ receptor gene polymorphism.

Conclusion : These results suggest that 267C/T polymorphism of 5 - HT₆ receptor gene is not significantly associated with susceptibility to TD in schizophrenia.

KEY WORDS : Tardive dyskinesia · Schizophrenia · Serotonin · Polymorphism · Genetics.

Department of Psychiatry, University of Soonchunhyang, College of Medicine, Seoul, Korea

Department of Psychiatry, Seoul National University, College of Medicine, Seoul, Korea

[†]교신저자 : , 140 - 743 657
) (02) 709 - 9234,) (02) 795 - 9959 E - mail) ha5hn@hosp.sch.ac.kr

서론

5-HT₆ mRNA가

¹⁴⁾ , Glazer ¹⁵⁾ D₂

5-HT_{2A}

가 , Ka-

pur ¹⁶⁾¹⁷⁾ clozapine risperidone

5-HT_{2A}

¹⁾

가 , Yassa Jeste ²⁾

5-HT₆

20~30%

(up-regulation),³⁾ GABA ⁴⁾

⁵⁾ ⁶⁾

가

⁷⁾

¹⁸⁾ 5-HT₆ 가

¹⁹⁾

가

³⁾⁸⁾

가

5-HT₆ (267C/

T)

clozapine

가 ⁹⁾¹⁰⁾

연구방법

1. 대상군 선정

가

가

가 , clozapine

가

가

가

Kusumi ¹³⁾

D₂

D₂

가

¹¹⁾¹²⁾

(Diagnostic and Statistical Manual of Mental Disorders, 4th edition)

5-HT_{2A}

가

2 DSM-60 가

60 가

2. 대상군 평가

가 (Abnormal Involuntary Movement Scale : AIMS²⁰)

가 AIMS 7가 가

AIMS

3. 유전자 분석 방법

Genomic DNA

EDTA K3가 가 1 (BD Vacutainer™) 5mL

(Wizard® Genomic DNA Purification Kit, Promega, WI, USA)

EDTA 1mL cell lysis solution 3mL 가 10 2000g 10 cell pellet nuclei lysis solution 1mL protein precipitation solution 330 μL 가 2000g 10 isopropanol 1mL 가 2000g 10 70% 1mL 가

pellet DNA rehydration solution 4C 8~12 가 65 1 가

DNA dNTP, Taq Polymerase가 AccuPower™ PCR PreMix (Bioneer co., Korea) 50 μL

300~700ng genomic DNA 50 pmole 가 Shin-kai²¹⁾

Forward primer 5' - TAg TCg CgC TCA TCT gCA CTC Ag - 3' , reverse primer 5' - CAg gAT CCT gCA gTA ggT gAA gC - 3'

GeneAmp PCR system 9600 (Perkin Elmer Cetus, USA)

95 5 1 , 95 45 , 62~70 45 , 72 45 30 touchdown PCR , 72 4

5 μL 2% agarose gel(SeaKem® LE agarose, FMCR, ME, USA) 100 volts 30 ethidium bromide DNA molecular size marker 497 bp 5 - HT₆

5 - HT₆ RsaI(Bioneer co., Korea) 1unit 가 37 8~12 , 3% agarose gel 371bp band 126bp band C/C , 497bp band T/T , 가 가 C/T

4. 통계학적 분석

SPSS(Statistical Package for Social Science) version 11.0 for Windows

가

Mann - Whitney U test² test가

가 267C/T 가

² test가 , 160 267C/T
2 , 267T 0.30
가

² test .

결 과

72 48
47.9 ± 10.7 (25~75) .
35 25 50.0 ± 11.0
, 37 23
45.7 ± 10.1
18.03 ± 8.93
17.12 ± 8.69
, 267C/T
AIMS 4.05 ± 5.33(C/C),
3.21 ± 3.87(C/T), 3.90 ± 3.00(T/T)
(p=0.724).
160 C/C 58 , C/T 52
T/T 10 . 267C/
T 가 (²=
1.746, d.f.=2, p=0.471),
(²=0.714, d.f.=1, p=0.398).

Table 1. Demographic characteristics of 120 schizophrenic subjects for 267C/T polymorphism of 5-HT₆ in Korean

	With TD (N=60)	Without TD (N=60)	p-value*
Gender(M/F)	35/25	37/23	0.709
Age(years)	50.1 ± 11.0	45.8 ± 10.2	0.056
Duration of illness (years)	18.0 ± 8.9	17.1 ± 8.7	0.597

* : p-value by Mann Whitney U test except gender with ² test

Table 2. Distribution of genotypes and Allele Frequencies of the 267C/T polymorphism of 5-HT₆ in Korean schizophrenics(% in parentheses)

	Genotypes*			Allele frequencies [†]	
	C/C	C/T	T/T	C	T
With TD [‡] (N=60)	28(47)	25(42)	7(11)	81(68)	39(32)
Without TD [‡] (N=60)	30(50)	27(45)	3(5)	87(73)	27(27)

* : ²=1.746, d.f.=2, p=0.471 using Fisher's exact test

† : ²=0.714, d.f.=1, p=0.398 using chi-square test

‡ TD : tardive dyskinesia

고 찰

가
5-HT₆ (267C/T)
D₃, ²² cytochrome P450 2D6²³
1A2²⁴ (CYP2D6 ; CYP1A2), manganese superoxide dismutase(MnSOD)⁷

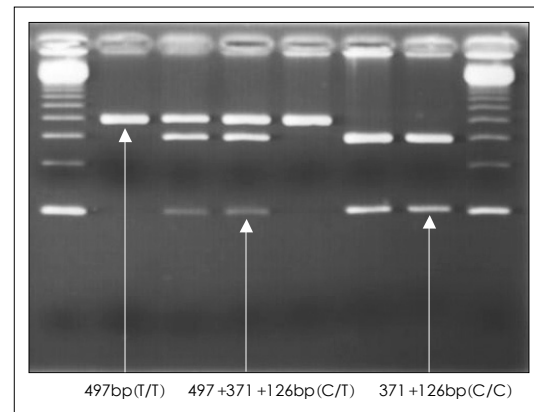


Fig. 1. An example of agarose gel analysis of restriction fragment length polymorphism pattern for 267C/T in 5-HT₆ receptor gene.

Table 3. Distribution of genotypes of 267C/T polymorphism in 5-HT₆ according to three AIMS* categories of patients with Tardive Dyskinesia in Korean schizophrenics(% in parentheses)

	Genotypes [†]		
	C/C	C/T	T/T
Orofacial type	11(44.0)	12(48.0)	2(8.0)
Distal type	15(53.6)	9(32.1)	4(14.3)
Trunk type	2(28.6)	4(57.1)	1(14.3)

*AIMS : Abnormal involuntary movement scale

† : ²=2.864, p=0.600 using Fisher's exact test

men ²⁵⁾²⁶⁾ 2C 2A Seg-
가
, Tan ²⁷⁾ 221
5-HT_{2A} 가
²⁸⁾가 5-HT_{2A} 가
102T/C 1438A/G
가 Basile
²⁹⁾ 5-HT_{2A}
, Chong ³⁰⁾ 5-HT₆
AIMS
5-HT₆ 267C/T
, Ohmori ³¹⁾ 5-HT₆ 267C/T
173
267C/T 가
267C/T 가가
Ohmori ³¹⁾ 가
1
AIMS 가 가
가 AIMS 가
, 267C/T 가 160 가
AIMS , 267C/T
. Ohmori ³¹⁾ AIMS
가 가
160 267T **결 론**
0.30 , ³²⁾
0.14 ³³⁾ **연구목적 :**
0.15
0.32, ³¹⁾
0.28³⁴⁾ 0.30
가 가

6

방 법 : 6

60 가

60 가

6 267C/T

가 (Abnormal Involuntary Movement Scale)

결 과 : 267C/T 가

가 6

결 론 : 6 267C/T

중심 단어 :

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