

정신분열병과 5-HT_{2A} / T102C 다형성의 관계*

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Association between Schizophrenia and the T102C Polymorphism of the 5-HT_{2A}*

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ABSTRACT

The 5-HT_{2A} receptor is of great interest for research into schizophrenia and psychopharmacology in light of the observation that schizophrenic patients has 5-HT cortical-subcortical imbalance and atypical antipsychotic clozapine has 5-HT_{2A} antagonists properties. An significant association between schizophrenia and the T102C polymorphism of the gene for 5-HT_{2A} receptor has been reported. In this study, we investigated an association between schizophrenia and the T102C polymorphism of the gene for 5-HT_{2A} receptor in Korean schizophrenic patients. The subjects consisted of 139 schizophrenic patients and 88 normal controls. Genomic DNA was amplified by PCR and digested with MsPI. The uncut product identified allele 1(nucleotide sequence TCT) ; digested products of 216bp and 156bp identified allele 2(nucleotide sequence TCC). The allele frequencies and the genotypic distribution of 5-HT_{2A} receptor gene were not significantly different between schizophrenic patients and normal controls. Since allele frequencies of the T102C polymorphism may differ between individuals of different ethnic backgrounds, it needs to be conducted in an advanced research.

KEY WORDS : 5-HT_{2A} · T102C polymorphism · Schizophrenia.

서 론

1995 ; Dean Hayes 1996). 5-HT_{2A} 가

5-HT₁

5-HT₄ 4 가 5-HT_{2A}(Chen 1992 ; Saltzman 1991), 5-HT_{2B}(Choi 1994 ; Kursar 1994 ; Schmuk 1994), 5-HT_{2C}(Saltzman 1991) 가 . 5-HT_{2A}

(Meltzer 1989). 5-HT_{2A} 13q14-q21

5-HT₂ 5-HT_{1A} 가 (Chen 1992 ; Hsieh 1990 ; Saltzman 1991), 13

가 가 (Breier 가 (Lin 1995). (Erdmann 1996 ; Inayam 1996 ; Williams 1996) 5-HT_{2A}

T102C

1997

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† : , 136 - 705 5가 126 - 1 5-HT_{2A} T102C (Hallmayer 1992 ; Hawi) (02) 920 - 5354,) (02) 923 - 3507

1997 ; Verga 1997),

HT_{2A}

T102C

5 -

Each Primer each 20pmol/50 μl

dNTP 200 μM

Taq polymerase 3U

Template DNA 200ng

연구대상 및 방법

1. 연구대상

DSM -

127

2. 연구방법

1) Genomic DNA의 정제

1.5ml 13,000rpm 1 pellet ACE shocking solution(NH₄Cl 8 g, Na₂EDTAH₂O 1g, KH₂PO₄ 0.1g 1l) 500 μl 3 2

pellet 400 μl nucleic lysis Buffer [Tris(pH 8.0) 10mM, NaCl 400mM, EDTA 2 mM] pellet 10% SDS 27 μl proteinase K 10 μl 가 56 2 saturated NaCl 135 μl 15 13000rpm 1 2 DNA DNA 70% 100 μl

2) 중합효소연쇄반응(Polymerase chain reaction : PCR)을 이용한 유전자형의 판별

5 - hydroxytryptamine type 2A nucleotide - 24 318 5 - hydroxytryptamine type 2A

Forward 5' - CGCCCGCCGCGCCCGCGCCCGTCCCGCCGTCTGCTACAAGTTCTGGCTT - 3'

Backward 5' - CTGCAGCTTTTCTCTAGGG - 3'

PCR 50 μl 3 35

Taq pol buffer 50mM KCl/10mM TrisCl(pH 8.3) MgCl₂ 1.5mM

50 μl

94 3 , 60 45 , 72 1 30 3 94 1 , 60 45 , 72 1 30 35

3) 증폭된 생성물의 분석

5 - hydroxytryptamine type 2A (TCT TCC : 102) PCR (372bp) MspI 5% polyacrylamide gel ethidium bromide (ultraviolet transilluminator) (polaroid, film 667)

4) Determination of PCR product

Size of product : 372bp Cutting with TaqI : Allele 1 - 372bp Allele 2 - 216bp, 156bp

3. 통계학적 분석

가 ² - test Hardy - We - inberg equilibrium ² - test p<.005

결 과

38.06 ± 11.46 63 , 37 35.97 ± 7.81 , 81 , 46 (1). 127 100 5 - HT_{2A} T102C (1). C1C1, C1C2, C2C2 가 59 (26%), 106 (46.7%), 62 C1C1, C1C2, C2C2 26 , 44 , 30 33 , 62 , 32 (² = .751, df = 2, p = .687)(2).

Table 1. Demographic characteristics of subjects

	Age (years)	Male	Female
Total (n=227)	36.89 ± 9.62	144	83
Schizophrenia (n=127)	35.97 ± 7.81	81	46
Controls (n=100)	38.06 ± 11.46	63	37

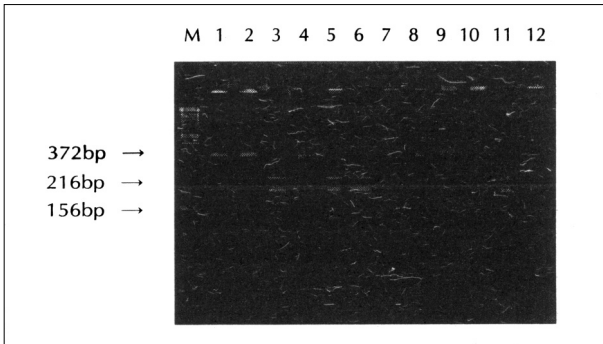


Fig. 1. PCR analysis of MspI RFLP in 5-HT_{2A} alleles for schizophrenics. 1 : c1c2 2 : c1c2 3 : c2c2 4 : c1c1 5 : c2c2 6 : c2c2 7 : c1c1 8 : c1c1 9 : c1c2 10 : c1c2 11 : c2c2 12 : c1c2 M : 100bp DNA size marker PCR products were run on 5% PAGE/0.5 × TBE gel

Table 2. Analysis of allelic and genotypic association of T102C poly-morphism

	Genotype frequency			Allele frequency		Hardy-Weinberg equilibrium
	C1C1	C1C2	C2C2	C1	C2	χ^2
Total (n= 227)	59	106	62	0.49	0.51	1.000
Normal (n=100)	26	44	30	0.48	0.52	1.406
Patients (n=127)	33	62	32	0.50	0.50	0.086

$\chi^2 = .751, df=2, p=.687$

고찰

5-HT_{2A} 가 (Erdmann 1996 ; Inayam 1996 ; Williams 1996).
 5-HT_{2A} Tsr25Asn, His452Tyr, 102T/C, 516C/T 4 가 (Tsr25Asn, His452Tyr) (102T/C, 516C/T) (Erdmann 1996).
 Erdmann (1996) Tsr25Asn, His452Tyr, 102T/C, 516C/T 4 5-HT_{2A} variant 102T/C
 5-HT_{2A} T102C linkage disequilibrium

functional 5-HT_{2A} receptor variant

Williams (1996) 5-HT_{2A} T102C linkage disequilibrium T102C 가 T102C 5-HT_{2A} mRNA (translation stage) 가 mutation(102T/C, 516C/T) 가 (Burnet Harrison 1995), promotor regions regulatory regions 가 5-HT_{2A} T102C 가 5-HT_{2A} T102C (Hallmayer 1992 ; Hawi 1997 ; Verga 1997) 5-HT_{2A} T102C 가 가 population stratification, (genetic heterogeneity), 가 (incomplete penetrance) 가 중심 단어 : 5HT_{2A} T102C
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