

한국인에서 조기-발병 및 후기-발병 강박장애 간의 Catechol-O-Methyltransferase 유전자 다형성 차이

천근아¹ · 김세주^{2,3} · 김찬형^{2,3}

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ABSTRACT

Difference of Val-158-Met Catechol-O-Methyltransferase Gene Polymorphism between Early- and Late-onset Obsessive-Compulsive Disorder in Korea

Keun-Ah Cheon, MD,¹ Se-Joo Kim, MD^{2,3} and Chan-Hyung Kim, MD^{2,3}

¹Department of Psychiatry, College of Medicine, Kwandong University, Goyang,

²Department of Psychiatry and ³Institute of Behavioral Science in Medicine, College of Medicine, Yonsei University, Seoul, Korea

Objective : Many researches strongly suggest that early- and late-onset obsessive-compulsive disorder (OCD) represent separate subtypes of the disorder, possibly with distinct underlying pathogeneses. The aim of this study was to determine the association between Val-158-Met Catechol-O-Methyltransferase (COMT) genotypes and the onset of OCD. **Method** : We recruited 124 OCD patients and classified them into an early-onset group (age of onset < 17 years) and a late onset-group (age of onset >17 years). From the blood, DNA was isolated using standard techniques and the COMT Val-158-Met polymorphism (H/H, H/L, and L/L) was genotyped. Each genotype consists of H (high activity) allele and L (low activity) allele. Genotype and allele frequencies of early- and late-onset OCD were analyzed by chi-square statistics. **Results** : The frequencies of H/H genotype and H allele in early-onset OCD group were significantly higher than late-onset OCD group (p=0.037 ; p=0.014). **Conclusion** : These results suggest that COMT gene polymorphism might be an important factor in the onset of OCD. (Korean J Psychopharmacol 2006;17(2):197-202)

KEY WORDS : COMT · Polymorphism · Early-onset · Late-onset · OCD.

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 : 2005 9 14 / : 2006 1 27
 교신저자 : , 135 - 720 146 - 92
 : (02) 2019 - 3340 · : (02) 3462 - 4304
 E - mail : spr88@yumc.yonsei.ac.kr
 essive - compulsive disorder) (hete-
 rogeneous) .^{1,2)}
 가
 가 .³⁾
 가 .⁴⁾

COMT

1)
 2) 가
 3) 가
 4) 가
 5) 가
 6) 가
 7) 가
 8) 가
 9-11) 가
 (tic disorder)
 12,13) 가
 14) 가
 COMT (Catechol - O - Methyltransferase)
 paminergic, noradrenergic system
 22q11
 SSRI
 13) COMT 가
 COMT Val -
 H/H , L/H
 allele
 H(high activity) allele
 L(low activity) allele
 L allele
 LL 가 가
 COMT

대상 및 방법

1. 연구대상

2002 3 2004 2 24

IV 2 DSM - 124 (15 - 17)

2. 연구방법

1) 정신과적 평가

SCID(Structured Clinical Interview for DSM - IV),¹⁸⁾

chorea가 가 , 6 가 ,

(Yale - Brown Obsessive - Compulsive Scale, Y - BOCS),¹⁹⁾ (Hamilton Depression Rating Scale, HDRS)²⁰⁾

2) Val-158-Met COMT 유전자 분석

124

4 , 120

(1) (Genotyping) Chip - based MALDI - TOF mass spectrometry platform(Sequenom, Inc., CA)

COMT

(2) (PCR) (PCR) (primer) 3

(forward primer) 5'-ACGTTGGATGACGTTG-GATGCACCTGTGCTCACCTCTCCT (reverse) 5'-ACGTTGGATGACGTTGGATGCATGCACACCTTGTCCTTCA

, 2.5 mM MgCl₂, 0.2 mM dNTP, 0.1 U HotStar Taq Polymerase(Quiagen GmbH, Germany) 100 nM, 4.0 ng genomic DNA가 5 ul 1X (TAKARA, Japan), 95 15 (denaturation), 45 cycles of 95 20 sec, 56 30 sec, 72 1 45, 3 72 (final extension)

(3) (homogeneous) MassEXTEND 0.3 U shrimp alkaline phosphatase 37 20, 85 5 (extension) 5'-CGGATGGTGGATTTTCGCTGGC. hME enzyme(Thermo-sequenase ; Amersham Pharmacia Biotech, UK), ACT termination mix, 5 uM 가 9 ul hME, 94 2, 94 5 sec, 52 5 sec, 72 5 sec 55 SpectroCLEAN(Sequenom, Inc., CA) (desalting), 384 well SpectroCHIP(Sequenom, Inc., CA) SpectroJET(Sequenom, Inc., CA) (spotting) SpectroCHIP MALDI - TOF MassARRAY system(Bruker - Sequenom, CA) (peak) (bad call sign)가 가 가

3) 자료분석

COMT (H/H, H/L, L/L)
(H, L) - -

H type(H/H+H/L) L type(L/L)

SPSS 11.5(Window version, Chicago, U.S.A.)
0.05

결 과

1. 조기 및 후기-발병 강박장애 군의 인구학적 결과

- 26.53 ± 7.97,
- 37.19 ± 11.07
- 13.30 ± 3.70,
- 27.58 ± 9.18
9.18 Y-BOCS HDRS 가 (1).

2. 조기 및 후기-발병 강박장애 군의 COMT 유전자형 및 대립형질 빈도

COMT Hardy - Weinberg Equilibrium ($\chi^2=1.19$, df=1, p=0.27, $\chi^2=$

Table 1. General and clinical characteristics of OCD patients according to age of onset

	Early-Onset OCD (N=60)	Late-Onset OCD (N=64)	p-value
Age	26.53 ± 7.97	37.19 ± 11.07	<0.01*
Onset of Age (years)	13.30 ± 3.70	27.58 ± 9.18	<0.01*
Sex	M 45 (75.0%) F 15 (16.7%)	M 38 (59.4%) F 26 (40.6%)	0.065**
Ill. Dur.	13.28 ± 8.30	9.47 ± 8.15	0.011*
Y-BOCS	27.37 ± 4.98	27.27 ± 6.34	0.934*
HDRS	15.00 ± 9.13	13.78 ± 10.17	0.562*

* : student t-test, ** : chi-square test, Ill. Dur. : Ill Duration, YBOCS : Yale-Brown obsessive compulsive symptom scale, HDRS : Hamilton depression rating scale

COMT

Table 2. Genotype and allele frequency of COMT gene polymorphism in early onset and late onset obsessive-compulsive disorder (OCD) patients

Genotype	Early onset OCD (N=60)	Late onset OCD (N=60)	Total OCD (N=120)	p- value
H/H	39 (60.9%)	25 (39.1%)	64	0.037*
H/L	17 (37.8%)	28 (62.2%)	45	
L/L	4 (36.4%)	7 (63.6%)	11	
H-type (H/H+H/L)	56 (51.4%)	53 (48.6%)	109	0.343
L-type (L/L)	4 (36.4%)	7 (63.6%)	11	
Allele	N=120	N=120		
H	95 (54.9%)	78 (45.1%)	173	0.014*
L	25 (37.3%)	42 (62.7%)	67	

* : p<0.05, chi-square test

0.04, df=1, p=0.84).

COMT H/H
39 (60.9%), 25 (39.1%), H/L 17
(37.8%), 28 (62.2%), L/L 4 (36.4%)
7 (63.6%)
($\chi^2=6.57$, df=2, p=0.037).

COMT H type(H/H+H/L) L type(L/L)
H type
56 (51.4%), 53
(48.6%) L type
4 (36.4%), 7 (63.6%)

($\chi^2=0.901$, df=1, p=0.343)(2). COMT (allele)
120
H 95(54.9%), L 25(45.1%)

H 78(37.3%), L 42(62.7%)
가 ($\chi^2=5.56$, df=1, p=0.014)(2).

고 찰

COMT Val - 158 - Met 3

가
(allele) H L
COMT
가
COMT
Hemmings
21)
15
COMT Dopamine
2 receptor gene(DRD2), Dopamine transporter gene
(DAT1), 5-HT2A, 5-HT1D
DRD4 7-repeat allele 가
COMT
COMT 가
COMT
25% H/H, 25% L/L,
50% H/L,²²⁾
COMT H/H 53.6%, H/L
35.4%, L/L 6%²³⁾
11.7% L/L 가
L/L²⁴⁾ 가
가
가
가

170 () 120 가
 COMT 가²⁷⁻²⁹⁾
 COMT COMT
 COMT
 COMT 가 가
 SSRI (false positive) 가 (bias)
 COMT 가
 COMT Val - 158 - Met H
 H/H
²⁵⁾
 H H/H 가 COMT 가
 가 가
 가 가
 COMT
 가 가

요 약

(serotonin transporter linked promotor regions ; 5-HTTLPR)
²⁶⁾
 가 5-HTTLPR 44bp COMT
 (long allele, l) (short allele, s)
 5-HT
 5-HTTLPR s/l
 l/l COMT (geno-
 SSRI typing) H/H L/H, L/L
 가
 가
 결 과 :

COMT

COMT	(H/H/, H/L, L/L)	
(H, L)		가
결론:	-	-
	가	가

중심 단어 : COMT

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