

한국인에서의 도파민 수송체 유전자 다형성  
(Dopamine Transporter Gene (DAT1) Polymorphism) 과  
사회공포증과의 연관성에 관한 예비 연구\*

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Polymorphism of Dopamine Transporter Gene(DAT1) in  
Korean Social Phobia Patients : Preliminary Study\*

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**ABSTRACT**

**O**bjective : Although polymorphism of dopamine transporter gene(DAT1) has been considered to be implicated in the pathogenesis of social phobia, previous investigations have been inconsistent and controversial. The authors investigated the relationship between DAT1 polymorphism and social phobia in Koreans.

**Methods** : DAT1 and alleles of fifty subjects who met DSM - IV criterion of social phobia, and those of age - & sex - matched fifty normal controls in Korea were compared. Additionally, patients were grouped into generalized(33) and nongeneralized(17) types and DAT1 polymorphism was compared with that of age - & sex - matched controls. DAT1 with variable number of tandem repeats(VNTR) were determined by using polymerase chain reaction. To compare the distribution of the DAT1 polymorphism between different groups, Fisher's exact test was used.

**Results** : There were no significant differences in either genotypic( $p=0.451$ ) or allelic( $p=0.452$ ) distributions between the social phobia patients and the controls. There also were no differences in genotypic distribution between subtypes of social phobia patients and the controls.

**Conclusion** : We couldn't find any association between DAT1 polymorphism and social phobia. Further studies including larger number of samples and diverse clinical variables should be conducted to elucidate the present findings.

**KEY WORDS** : Social phobia · Dopamine transporter gene(DAT1) · Polymorphism · Association study.

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서 론

6-10) 5p 15.3  
 15 exon 15 exon  
 (3'-untranslated region : 3'-UTR, SLC6A3)  
 40  
 variable number of tandem repeats(VNTR)  
 11-13)

DSM - (1980)

가 ,  
 Kendler <sup>1)</sup> 가 <sup>14-17)</sup>  
 30~40%가  
 Stein <sup>2)</sup> 가 (generalized type) 가 . Vandenberg <sup>18)</sup>  
 가 .  
 , Michelle <sup>19)</sup> 10 -  
 52% 100%  
 , Nakatome <sup>20)21)</sup>  
 10 - 가 90%

가 (monoamine  
 oxidase inhibitors, MAOIs)가  
<sup>3)</sup>  
 (single photon emission computed tomography :  
 SPECT)  
 가 <sup>4)</sup> D2 (DRD<sup>2)</sup>  
 (binding potential) <sup>5)</sup>

연구 방법

1. 연구대상 ( 1)

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Table 1. Demographic characteristics of patients

Demographic data	All social phobia patients(n=50)	Generalized social phobia patients(n=33)	Nongeneralized social phobia patients(n=17)
Male/Female (N)	31/19	19/14	12/5
Mean Age ± SD (years)	29.64 ± 8.25	27.52 ± 7.87	33.76 ± 7.55
Comorbid Diagnosis by DSM-IV & M.I.N.I. (N)			
Dysthymia	8	6	2
Obsessive compulsive disorder	5	5	0
Generalized anxiety disorder	1	1	0
Bipolar I disorder	1	1	0
Panic disorder	1	1	0
Alcohol abuse	1	1	0

DSM-IV : Diagnostic and statistical manual of mental disorder IV,  
 M.I.N.I. : Mini international neuropsychiatric interview

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

가  
Mini International Neuropsychiatric Interview(M.I.N.I.)

50  
21 , 32.04 ± 8.27  
(nongeneralized type)  
33 , 19 , 14  
30.61 ± 7.50 , 17  
17 , 12 , 5  
33.71 ± 7.20

## 2. DAT1 유전자형 확인

### 1) Genomic DNA의 정제

5ml 3,000rpm 10  
pellet ACE shocking  
solution(NH<sub>4</sub>CL 8g, Na<sub>2</sub>EDTAH<sub>2</sub>O 1g, KH<sub>2</sub>PO<sub>4</sub> 0.1  
g 1l ) 5ml 3  
2  
pellet 3ml  
nucleic lysis buffer[ Tris(pH 8.0) 10mM, NaCl 400  
mM, EDTA 2mM] pellet  
10% SDS 200 μl proteinase K 10 μl 가  
56 2 saturated NaCl  
1ml 15 . 13,000rpm  
1 2  
DNA

DNA 70%  
100 μl

### 2) 중합효소연쇄반응(Polymerase Chain Reaction : PCR)을 이용한 유전자형의 판별

DAT 40bp nucleotide repeat polymorphism

5 ' - TGT GGT GTA GGG AAC GGC CTG AG - 3 '  
5 ' - CTT CCT GGA GGT CAC GGC TCA AGG - 3 '  
25 μl 12.5 μl GC buffer(Takara, Japan), 1.5U Taq polymerase(Takara, Japan), 10pmol/25 μl , 2.5mM dNTP(4 μl), 200ng template DNA . 94 5  
(denaturation) , 94  
30 , 60 30 , 72 30 35  
extension 72 5  
. 2% agarose gel ethidium bromide (ultraviolet transilluminator) polaroid (polaroid, film 667) ( 1).

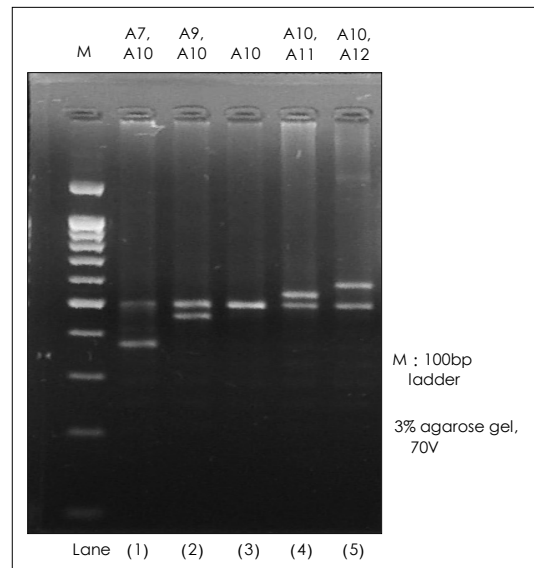


Fig. 1. Separation of PCR-amplified allelic variants at the DAT1 VNTR locus by agarose gel electrophoresis and ethidium bromide staining. Approximate size : lane 1= 360/480bp ; 2=440/480 ; 3=480 ; 4=480/520 ; 5=480/560. M=100-Base-Pair Ladder Marker.

### 3. 통계분석

Fisher's exact test

가 Fisher's exact test

Diagnostics program HWDIAG v. 1.0

SPSS 11.0 for Windows

,  $p < 0.05$

### 결 과

86%,  
84%가 10/10,  
가 (p=0.451)( 2).  
93%, 92%가 10-  
가,  
(p=0.452)( 3).  
Hardy - Weinberg equilibrium  
(p=0.91), (p=0.88)

**Table 2.** Dopamine Transporter Gene(DAT1) genotype frequencies in 50 social phobia patients and in age-, sex-matched 50 normal controls

	DAT1 Genotype					Total
	7/10	9/10	10/10	10/11	10/12	
Patients	3(6)	2(4)	43(86)	2(4)		50(100)
Controls	3(6)	4(8)	42(84)	1(2)		50(100)

Figures in parentheses are percentages  
 $\chi^2 = 3.678$ ,  $df = 4$ ,  $p = 0.451$

**Table 3.** Allele frequencies of the Dopamine Transporter Gene(DAT1) in 50 social phobia patients and in age-, sex-matched 50 normal controls

	Allele					Total
	7	9	10	11	12	
Patients	3(3)	2(2)	93(93)	2(2)		100(100)
Controls	3(3)	4(4)	92(92)	1(1)		100(100)

Figures in parentheses are percentages  
 $\chi^2 = 3.672$ ,  $df = 4$ ,  $p = 0.452$

Hardy - Weinberg

(p=0.112)

(p=0.119)

( 4, 5),

(p=0.832)

(p=0.840)

가 ( 6, 7).

**Table 4.** Dopamine Transporter Gene(DAT1) genotype frequencies in 33 generalized social phobia patients and in age-, sex-matched 33 normal controls

	DAT1 Genotype					Total
	7/10	9/10	10/10	10/11	10/12	
Patients	2(6.1)		29(87.9)	2(6.1)		33(100)
Controls	3(9.1)	4(12.1)	25(75.8)		1(3)	33(100)

Figures in parentheses are percentages  
 $\chi^2 = 7.496$ ,  $df = 4$ ,  $p = 0.112$

**Table 5.** Allele frequencies of the Dopamine Transporter Gene(DAT1) in 33 generalized social phobia patients and in age-, sex-matched 33 normal controls

	Allele					Total
	7	9	10	11	12	
Patients	2(3)		62(93.9)	2(3)		66(100)
Controls	3(4.5)	4(6)	58(87.9)		1(1.5)	66(100)

Figures in parentheses are percentages  
 $\chi^2 = 7.333$ ,  $df = 4$ ,  $p = 0.119$

**Table 6.** Dopamine Transporter Gene(DAT1) genotype frequencies in 17 nongeneralized social phobia patients and in age-, sex-matched 17 normal controls

	DAT1 Genotype					Total
	7/10	9/10	10/10	10/11	10/12	
Patients	1(5.9)	2(11.8)	14(82.4)			17(100)
Controls	1(5.9)	1( 5.9)	15(88.2)			17(100)

Figures in parentheses are percentages  
 $\chi^2 = 0.368$ ,  $df = 2$ ,  $p = 0.832$

**Table 7.** Allele frequencies of the Dopamine Transporter Gene(DAT1) in 17 nongeneralized social phobia patients and in age-, sex-matched 17 normal controls

	Allele					Total
	7	9	10	11	12	
Patients	1(2.9)	2(5.9)	31(91.2)			34(100)
Controls	1(2.9)	1(2.9)	32(94.1)			34(100)

Figures in parentheses are percentages  
 $\chi^2 = 0.349$ ,  $df = 2$ ,  $p = 0.840$

고찰

Rowe<sup>15)</sup> quantitative transmission disequilibrium test(QTDT) (internalizing disorder) 가 가 (population stratification).

Patrick<sup>16)</sup> 10- (novelty seeking) 가 Terwilliger<sup>26)</sup> haplotype - based haplotype relative risk method Cook<sup>27)</sup> haplotype relative risk 10- 가 (haplotype) 가

Blum<sup>14)</sup> / (schizoid/avoidant behavior : SAB) D2 10- 가

2)22) 가

Kennedy<sup>17)</sup> 17 가 (linkage analysis) 가 , 2001 가

23) 1) 가

3-, 5-, 7-, 8-, 9-, 10-, 11-, 12-, 13- (popula- tion-based association study) - 가 가 9- 10- 95.5% 480 10- (case - control study) 가 92% , 12 가 10/11 Rivest<sup>24)</sup> (striatum) (substantia nigra) 가

가

35-37)

가 10-

29)

가 가 , 가

9- 가

가

가 Jacobsen

가 가

### 결 론

1

가

50

33 , 17

가

가

(nicotine)

가

가

가

30)31)

중심 단어 :

(DAT1)

(severity)

가

32)

가

(binding availability)

Heinz

33) 9/10

(heterozygous)

가 10/10

(homozygous)

가

, Jacobsen 34) 10-

가

, Jacobsen

가

&

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