

# Association study of the Serotonin Transporter, Serotonin 2A Receptor Gene and ADHD in Korean Children

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**Purpose** ; Attention-deficit/hyperactivity disorder(ADHD) is one of the most common childhood psychiatric disorders. The evidences from family, twin, adoption studies suggests that ADHD is a highly heritable disorder. Although many reports have shown the genetic association between ADHD and dopaminergic/noradrenergic system, the number of the reports about the genetic association between ADHD and serotonergic system was relatively low. The aim of this study was to investigate the association between Korean ADHD children and 1) the I/s polymorphism of serotonin transporter linked polymorphic region(5-HTTLPR), 2) the T02C polymorphism of serotonin 2A receptor(5-HTR2A).

**Methods** ; The study sample consisted of 189 Korean ADHD children diagnosed by Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version-Korean Version(K-SADS-PL), both parents of ADHD children, and 150 normal children. DNA were extracted from the blood of all samples, and genotyping was done. Based on the allele and genotype information, not only the case-control analysis between ADHD and normal children but also the family-based association test among ADHD children and their both parents were performed. Transmission disequilibrium test(TDT) was used for family-based association test. The results of the clinical rating scales and neuropsychological tests were compared according to the genotype of ADHD children.

Characteristics	Cases (N=189)		Controls (N=150)	
Age (years)	9.2 ± 2.3		9.4 ± 0.6	
IQ	105.0 ± 14.6		100.5 ± 8.5	
	(N)	(%)	(N)	(%)
<b>Sex</b>				
Male / Female	166/23	87.8/12.2	131/19	87.3/12.7
<b>ADHD subtype</b>				
Combined	115	60.8	-	-
Inattentive	32	16.9	-	-
Hyperactive-impulsive	15	7.9	-	-
NOS	27	14.3	-	-
<b>Comorbid disorder</b>				
Oppositional defiant dis.	18	9.5	-	-
Conduct disorder	2	1.1	-	-
Mood disorder	3	1.6	-	-
Anxiety disorder	6	3.2	-	-
Enuresis	6	3.2	-	-

Table 1. Demographic / Clinical characteristics

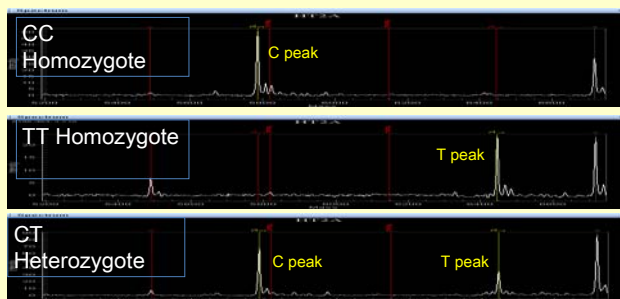


Fig 1. SNP genotyping mass spectra generated using matrix assisted laser desorption/ionisation-time of flight(MALDI-TOF) mass spectrometry for the 5-HT2A receptor gene

**Results** ; 1) By case-control analyses, there were no statistically significant differences in the genotype and allele frequencies of I/s polymorphism between ADHD and normal children. But after classifying each ADHD and normal children by the existence of C allele in T102C polymorphism, there were statistically significant differences in the genotype frequencies between ADHD [ 78.5%(genotype with C allele) vs. 21.5%(genotype without C allele)] and normal children [68.0%(genotype with C allele) vs. 32.0%(genotype without C allele)]( $\chi^2=4.73$ ,  $p=.030$ ).

1	Proband (N=186)		Control (N=150)		p value
	n	%	n	%	
<b>Genotype</b>					
T/T	40	21.5	48	32.0	.078
T/C	104	55.9	69	46.0	
C/C	42	22.6	33	22.0	
<b>Allele</b>					
T	184	49.5	165	55.0	.153
C	188	50.5	135	45.0	

2	Proband (N=186)		Control (N=150)		p value
	N	%	N	%	
<b>Genotype Group I</b>					
with T allele	144	77.4	117	78.0	.899
without T allele	42	22.6	33	22.0	
<b>Genotype Group II</b>					
With C allele	146	78.5	102	68.0	.030*
without C allele	40	21.5	48	32.0	

Table 2. All ADHD vs. Controls, 5-HT2A Rc. T102C polymorphism \* ;  $\chi^2=4.73$

2) In family-based association study, TDT failed to detect linkage disequilibrium(LD) between 5-HT2A gene polymorphism and ADHD in whole ADHD families. However, in the families of ADHD inattentive type(N=23), I allele of 5-HTTLPR was transmitted more preferentially in the ADHD probands even if the number of families was low. ( $\chi^2=4.57$ ,  $p=.032$ )

Not transmitted	I	Transmitted	
		I	s
	s	4	3
		11	28

Table 3. Families with inattentive type, 5-HTTLPR polymorphism (Number of trio = 23)

McNemar's  $\chi^2$  test ;  $\chi^2 = 4.57$ ,  $df=1$ ,  $p=.032$

**Conclusion** ; The significant association between ADHD and 5-HTR2A T102C gene polymorphism was confirmed by case-control analysis, even if the family-based association study failed to detect significant results. Those results prove the genetic association between the 5-HTR2A T102C gene polymorphism and Korean ADHD children. And those suggest the possibility of the important interaction between the serotonergic and dopaminergic system in the pathophysiological or the pharmacological treatment mechanism of ADHD.

## Reference

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