Association of HTR2A rs7322347 polymorphism with youth onset schizophrenia

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Objective: We investigated the associations of rs7322347 5HT2A with youth onset schizophrenia in the Russian population in a case-control study, and the role of the genotype in the severity of clinical features.

Materials and methods: A total of 380 (186 male, 194 female, mean age 32.6 ± 11.6) healthy volunteer controls and 215 (103 male, 112 female, mean age 32 ± 8.4) patients who gave their consent to participating and met the inclusion criteria of youth onset schizophrenia (before 26 years old), participated in the study. All participants were biologically unrelated Caucasian people. Subjects were recruited from N. A. Alekseev Psychiatric Hospital No. 1, Moscow, Russia. Current patient symptomatology was assessed using the DSM V. Patients were evaluated using a structured interview for the Positive and Negative Syndrome Scale (PANSS), the mean sum of PANSS scores was 104.15 ± 30.67 .

Genotyping: SNP were typed using predesigned TaqMan SNP genotyping assay, following the manufacturer's instructions (Applied Biosystems, Thermo Fisher, USA). PCR and allelic discrimination assays were run using a QuantStudio 5 RealTime PCR system (Applied Biosystems, Thermo Fisher, USA).

Results: Genotype frequencies in all groups followed the Hardy-Weinberg equilibrium.

Analysis revealed significant gender specific associations between studied polymorphism and youth onset schizophrenia ($p = 0,0001$). Gender stratification showed that association with disease risk was significant for rs7322347 in male subjects (Table 1).

Analysis of the association between genotype and schizophrenia symptoms has been provided for male and female groups separately. In males, differences were found on the PANSS scale for P1 ($F = 10.1$ $p = 0.002$) and G7 ($F = 5.62$, $p = 0.02$). In females, differences were found in the symptom P7 "hostility" ($F = 6.95$, $p = 0.01$). The association remained statistically reliable after Bonferroni correction.

Thus, the presence of allele T is associated with an increase in certain symptoms of schizophrenia in both male and female.

The main statistically significant results are presented in Table 2.

rs	Allele	Case frequency	Control frequency	χ^2	p	OR	[95% CI]
rs7322347 5HT2A	A	0,419	0,314	23,01	0,000002	1,58	1.33– 2.16
Chromosome 13	T	0,581	0,686			0,63	0.50 – 0.80
Male	A	0,42	0,308	9,88	0,002	1,63	1.20 – 2.21
	T	0,58	0,692			0,61	0.45 – 0.83
Female	A	0,419	0,345	1,8	0,18	1,37	0.87 – 2.15
	T	0,581	0,655			0,73	0.46 – 1.15

Table 1. Distribution of 5HT2A polymorphism in youth7onset schizophrenia and control groups

Scale		5HT2A (Male)		5HT2A (Female)	
		F	p	F	p
PANSS	PI. Dellusions	10,1	0,002	0,03	0,86
	P7. Hostility	0,83	0,37	6,95	0,009*
	G7. Motor retardation	5,62	0,020	0,01	0,92

Table 2. Association between genotype and schizophrenia symptoms

Conclusions:

The association between rs7322347 and schizophrenia ($p=0.000002$) is described for the first time

The severity of some symptoms depends on the combination of gender and allelic state of 5HT2A rs7322347