

Genetic linkage and association studies of schizophrenia and related disorders using dopamine transporter gene markers

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The dopamine transporter (DAT) is primarily responsible for terminating dopaminergic activity at the synaptic level. The human DAT gene, located on chromosome 5p15.3 (Vandenberg et al., 1992a), displays polymorphic VNTRs (Vandenberg et al., 1992a) and *TaqI* RFLPs (Vandenberg et al., 1992b).

Potential involvement of DAT gene variants in the etiology of schizophrenia spectrum disorders was tested using these polymorphic DAT gene markers in 156 subjects from 16 multiplex pedigrees with schizophrenia, schizophreniform, schizoaffective, schizotypal disorders and mood incongruent psychotic depression. Complete ($\theta=0.0$) linkage to the schizophrenia spectrum was excluded under both dominant and recessive models in these pedigrees (Table 1).

However, given the likely heterogeneity of schizophrenia's genetic underpinnings, we are in the process of replicating these findings in a large Italian pedigree (family F05 in Macciardi et al., 1992), while performing an association study on 200 patients to assess whether DAT gene variants may possibly contribute to clinical features of specific schizophrenia subtypes.

Table 1. Lod scores at the dopamine transporter locus for 16 pedigrees with schizophrenia

Model	Pene.	Allele freq.	Recombination fraction					
			0.00	0.05	0.10	0.20	0.30	0.40
DOM SS	50%	0.015	-6.03	-2.40	-1.22	-0.34	-0.15	-0.10
	1%		-4.19	-1.91	-1.04	-0.35	-0.14	-0.07
DOM SZ	50%	0.0085	-4.53	-1.61	-0.82	-0.23	-0.08	-0.05
	1%		-2.77	-0.97	-0.45	-0.10	-0.04	-0.03
REC SS	50%	0.172	-3.18	-0.50	0.37	0.73	0.47	0.13
	1%		-0.66	-0.01	0.27	0.37	0.22	0.06
REC SZ	50%	0.130	-4.12	-1.30	-0.46	0.05	0.06	-0.01
	1%		-1.28	-0.59	-0.26	-0.02	0.01	-0.01

DOM, dominant; REC, recessive; SS, schizophrenia spectrum disorder; SZ, pure schizophrenia; Pene., penetrance; Allele freq., disease allele frequency.

References

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