Cross-disorder genetic analysis of Tics, Obsessive Compulsive and Hoarding Symptoms

Nederlands Tweelingen Register

N. R. Zilhão[1], D.C. Cath[1] , D. J. A. Smit[2], D. I. Boomsma[2]

[1] *Department of Clinical and Health Psychology, Utrecht University and Altrecht Academic Anxiety Disorders Center, Utrecht, the Netherlands.*
[2] *Department of Biological Psychology, VU University, Amsterdam, Amsterdam, the Netherlands*

Introduction

Hoarding, Obsessive-Compulsive Disorder and Tic disorders are comorbid psychiatric disorders. This overlap may be the result of shared genetic variation. Population based twin studies have found significant genetic correlations between hoarding and OC symptoms (OCS), with correlations varying between 0.1 and 0.45. Research exploring the relationship between tics and OCD have failed to detect shared variation. Here our aim was to extend current knowledge on the genetic structure underlying hoarding, OC symptoms and tics to assess the degree which genetic factors contributing to the etiology of these disorders are shared.

Methods

Participants

Participants were twins from the Netherlands Twin Register, who completed self-report Questionnaires: N=7482(2300m/5182f) individuals with OCS data (PI-ABBR), N=7605 (2337m/5268f) with Hoarding (HRS-SR), and N=7838 (2435m/5403f) with tics (YGTS), from a total of 5337 families. The final selection included in the analysis comprised 1514 monozygotic (MZ) and 1196 dizygotic (DZ) twin pairs (mean age=33.61 years).

Analysis

Genetic analysis were conducted using the software Mplus, fitting a trivariate model with liability thresholds for all phenotypes. For each phenotype a categorical variable was defined from cut points on the total scores of the full distribution of the data, representing the true underlying susceptibility to disease in the population.

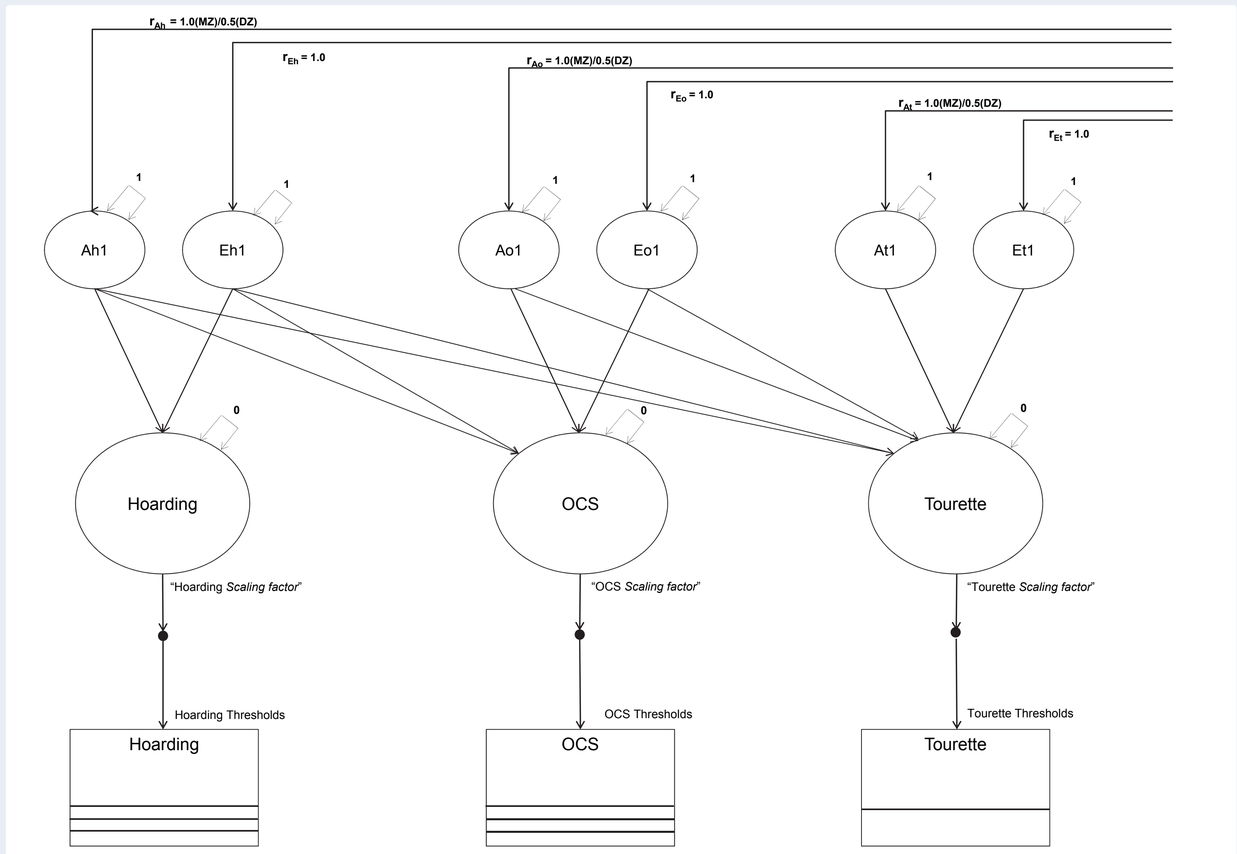

Figure 1. Trivariate twin model. Squares represent observed categorical variables and circles latent estimated parameters. Model representation of one twin.

Results

- From the total sample, 4.7% had hoarding over the clinical cutoff level (HRS-SR over 17), 6.0% for OCS (PADUA score>16), and 12.8% reported one or more of tic disorders as in the YGTS.
- The prevalence rates were similar for both genders. No sex-specific or twin-specific environment was found.
- MZ twin correlations were consistently around twice the DZ correlations (Table 1) suggesting additive genetic influence for all traits.
- For all phenotypes, genetic factors accounted for 32-38% of the total phenotypic variance (Table 2).
- Bivariate analysis showed genetic contributions of 50.4 % (Hoarding & OCS), 70,1% (Hoarding & tics) and 61,1% (OCS & tics) to the shared phenotypic variance among the phenotypes (Table 2).
- The cross-trait genetic correlations were **0.41** (hoarding and OCS), **0.352** (hoarding and tics) and **0.367** (OCS and tics).

Table 1. Twin polychoric correlations for Hoarding, OCS and tics. MZ, monozygotic; MZM, monozygotic male ; MZF, monozygotic female; DZ, dizygotic; DZM, dizygotic male; DZF, dizygotic female; DOS, dizygotic oppposite sex.

	MZ	MZM	MZF	**DZ**	DZM	DZF	DOS
Hoarding	**0.336**	0.379	0.325	**0.177**	0.247	0.151	0.048
OCS	**0.384**	0.379	0.386	**0.177**	0.197	0.139	0.214
tics	**0.370**	0.242	0.414	**0.190**	0.338	0.172	0.114

Table 2. Trivariate genetic model for Hoarding, OCS and TS. h^2, heritability. 'proportion genetic' indicates the proportion of the phenotypic correlation between the traits that is due to genetic factors.

		phenotypic correlation		proportion genetic		genetic correlation	
	h^2	Hoarding	OCS	Hoarding	OCS	Hoarding	OCS
Hoarding	32.6%	-		-		-	
OCS	37.5%	0.298	-	0.504	-	0.410	-
tics	36.7%	0.151	0.245	0.701	0.611	0.352	0.367

Discussion

Our heritability estimates show a substantial contribution of genetic factors to the phenotypic variance for the three phenotypes, corroborating what is described in the literature.

The trivariate results provide new evidence regarding the shared genetic etiology underlying the phenotypes. We observed a significant contribution from genetic factors to the phenotypic covariance between the phenotypes (0.50-0.70). Furthermore, genetic correlations reveal a considerable genetic overlap (0.35 – 0.41). These results suggest that the comorbidity between Hoarding, OCD, and tics is to a large extent caused by an overlap in genetic variation. This has strong implications in designing future genetic studies. Our findings show that the benefits in power from increased sample sizes would outweigh the losses due to disease heterogeneity, considering the observed genetic correlations.

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