Genetic Factors Underlie Stability of Obsessive–Compulsive Symptoms

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The contribution of genetic and environmental factors to the stability of obsessive–compulsive (OC) symptoms has not yet been established in adult population based samples. We obtained the Young Adult Self Report Obsessive–Compulsive Subscale in mono- and dizygotic twins from the population-based Netherlands Twin Register in 1991, 1995 and 1997 and the Padua Inventory Revised Abbreviated in 2002. Stability of OC symptoms was analyzed as a function of genetic and environmental components. Heritability of OC behavior was around 40% at each time-point, independent of the instrument used. OC behavior was moderately stable with correlations ranging between $r = .2$ (for 11-year intervals), .4 (for 4–5 year intervals) and .6 (for 2 year intervals). Genetic correlations across time were higher, varying between .4 and .9, indicating that the stability of OC symptoms is mainly due to stable genetic factors. This study showed a moderate heritability and stability for OC behavior in adults. Genetic stability across time is high.

Keywords: obsessive–compulsive disorder, OCD, OC symptoms, twin study, twins, longitudinal

Research on persistence of obsessive–compulsive disorder (OCD) and/or Obsessive-Compulsive (OC) symptoms has mainly concentrated on subjects who are patients. Several older studies on the course of OCD have suggested it to be chronic and lifelong with a waxing and waning course (for a review see Goodwin et al., 1969). More recent studies on the course of OCD obtained varied results; some concluded that OCD is a chronic illness with low rates of remission (Alonso et al., 2001; Eisen et al., 1999; Rasmussen & Tsuang, 1986), whereas other studies found that about 50% of patients remit (Angst et al., 2004; Orloff et al., 1994; Reddy et al., 2005; Skoog & Skoog, 1999; Steketee et al., 1999). Reddy et al. (2005) concluded that poor outcome in previous studies may have been due to the inclusion of severely and chronically ill patients.

Stewart et al. (2004) conducted a meta-analysis of the long-term course in clinical cases of paediatric OCD and found persistence rates of 41% for full OCD and 60% for full or subthreshold OCD. Only two studies examined OCD and OC symptoms in a community cohort. The Zurich community cohort study (Angst et al., 2004) followed a group of adolescents for almost 20 years. Although the course of OC symptoms was described as chronic by 60% of the subjects, symptoms ameliorated in most of them. Fullana et al. (2007) examined the temporal stability of obsessive–compulsive dimensions over a period of two years, using the Obsessive–Compulsive Inventory — Revised (Foa et al., 2002). In a nonclinical sample of 132 undergraduate students, they found no significant changes in symptoms dimensions scores between the baseline and follow-up, except for the Obsession scale.

These data provide a longitudinal perspective on OCD and OC symptoms, but do not address the etiology for the observed stability. We examined stability of OC symptoms as a function of stable genetic influences in children (van Grootheest et al., 2007a) and found that OC symptoms, as measured by the Obsessive-Compulsive Scale of the Child Behavior Checklist (CBCL-OCS) (Hudziak et al., 2006; Nelson et al., 2001), are moderately stable. In children the correlations across ages 7, 10 and 12 years were .5. Around 40% of the stability in OC behavior was explained by genetic factors and the remaining of the variation was explained by shared and non-shared environment.

The purpose of the present study is to explore the stability of OC symptoms in adults across a period of 11 years and to determine the genetic and environmental contributions to stability of OC symptoms using longitudinal OC symptom data from a large sample of twins. OC symptoms were assessed in 1991, 1995, 1997 and 2002.

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Methods and Materials

Subjects and Procedure

This study is part of a longitudinal survey study in twin families registered with the Netherlands Twin Register (Boomsma et al., 2002b; Boomsma et al., 2006). Since 1991, every two to three years twin families receive a survey by mail containing questionnaires about health, personality and lifestyle. For the present study, we included OC data of adolescent and adult twins from 1991, 1995, 1997 and 2002. Table 1 gives an overview of the number of complete and incomplete twin pairs included in the study, at each occasion. The total sample consists of twins from 4198 families. There were 441 twin pairs who participated four times; 734 twin pairs participated three times; 1102 twin pairs participated twice and 1921 twin pairs participated once. If twins did not respond at a particular time point they were approached for the next mailing. Twins participating 4 times did not have a significantly different score on OC symptoms than twins who participated once ($p = .58$). In 1991 and 1995, adolescent and young adult twins were recruited through City Council Registrations. From 1997 onwards an additional effort was made to recruit older twins for the study. This effect is reflected by the mean ages per time-point, which were 17.8 (SD 2.3) in 1991, 19.8 (SD 3.2) in 1995, 25.5 (SD 9.8) in 1997 and 33.0 (SD 13.5) in 2002.

Zygosity of the twins was determined using items about physical similarity and the frequency of confusion of the twins by family and strangers. For 869 same sex twin pairs, zygosity information was available from DNA polymorphisms. The agreement between zygosity information from the questionnaire and DNA data is 97% (Willemsen et al., 2005).

Measures

In 1991, 1995 and 1997, OC symptoms were measured with the Young Adult Self Report Obsessive–Compulsive Scale (YASR-OCS) (van Grootheest et al., 2007b). In 2002, OC symptoms were measured with the Padua Inventory abbreviated (PADUA ABBR) (Cath et al., 2008).

The YASR is a standardized self-report questionnaire for adolescents and adults (Achenbach, 1997). It comprises 110 problem items, covering emotional and behavioral problems during the previous 6 months. The participants respond on a 3-point scale (0, not true, 1, somewhat or sometimes true, and 2, very true or often true). The YASR-OCS contains eight OC items and is similar to the CBCL-OCS (Geller et al., 2006; Hudziak et al., 2006; Nelson et al., 2001). A total score is obtained by summing the scores on the relevant eight items, thus creating a score range between 0 and 16. Using a cut-off of 7, 82.4% of all DSM-determined OCD cases were identified in a clinical sample of children with a specificity of 69.7% (van Grootheest et al., 2007b). Cronbachs' α of the scale was .69.

The Padua Inventory abbreviated (PI-R ABBR) (Cath et al., 2008) has been derived from the Padua Inventory — Revised (PI-R), which is a widely used self-report inventory on obsessive-compulsive symptoms (Oppen van, 1992; Sanavio, 1988). The PI-R contains 41 items that measure OC symptoms on a 0–4 scale, and contains five subscales, that is, washing, checking, rumination, precision and impulses (Oppen van et al., 1995). For the aim of this study, the PI-R was reduced to 12 items. Item choice was based on two items of each subscale with highest factor loadings in a previous validation study (Oppen van et al., 1995), and with one additional item for each of the more equivocal obsession subscales rumination and impulses. Cronbachs' α of the scale was .73, which is an indication of reasonable internal consistency. Sensitivity and specificity of the PI ABBR to detect DSM IV OCD was 74% and 72% respectively, when compared to clinical controls (Cath et al., 2008).

Analyses

Analyses were conducted using structural equation modeling, with the statistical software package Mx (Neale et al., 2006). In longitudinal studies, usually not all subjects take part in the study at all occasions. To be able to use all data, full-information maximum likelihood estimation with raw data was used. The fit of different models was compared with likelihood-ratio tests, by subtracting –2LL for a restricted nested model from –2LL of a less restricted model. The resulting test statistics has a χ^2 distribution with degrees of freedom (df) equal to the difference of the df between the models. The saturated model, a model in which the covariance matrix among twins and the mean structures are computed without any restriction, was used as a reference to test for the homogeneity of means and variances in monozygotic (MZ) and dizygotic (DZ) twins and in men and women. The type-I error rate of all statistical tests was set at .01 to accommodate multiple testing.

Genetic Modelling

Twins may resemble each other because they share their pre-and postnatal environment, often referred to as shared or common environment (C). In addition, MZ / DZ twins may resemble each other because they share 100% / 50% of their additive genetic variance (A). Thus, additive genetic factors are correlated 1 in MZ and .5 in DZ pairs. Shared environmental factors are correlated 1 for MZ and DZ twins. Non-shared factors (E) refer to individual experiences and are uncorrelated for MZ and DZ twins by definition (Boomsma et al., 2002a).

To analyze the longitudinal data, a simplex model or transmission model was employed, which is a developmental model that explains the pattern of correlations across time-points. The simplex model is suitable for longitudinal data in which there is occasion-to-occasion transmission causing correlations to decrease with increasing distances between time-points
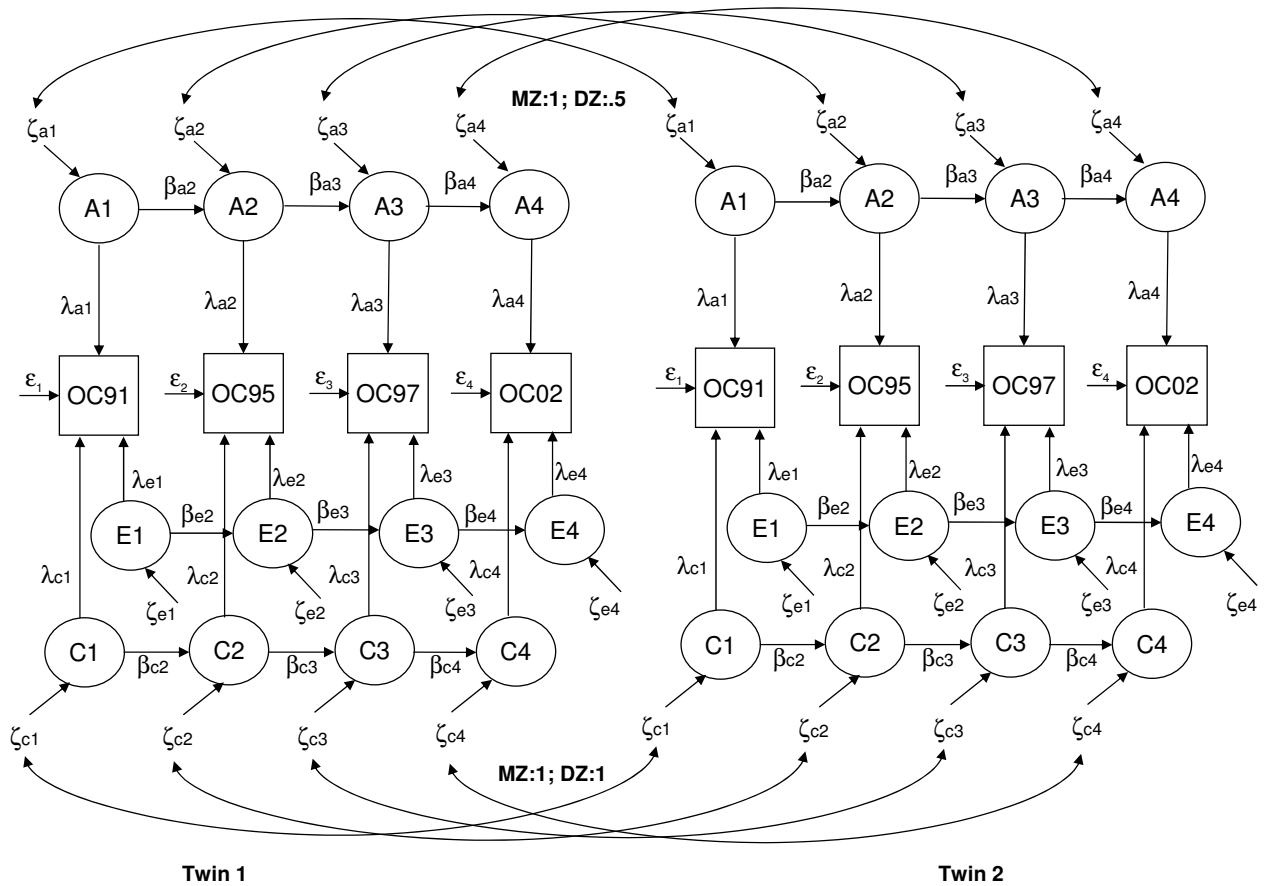
Figure 1

Full ACE simplex model for the observed variable OC symptoms (squares), which is measured across four time-points (OC91, OC95, OC97 and OC02). The loadings of the observed variables on the latent factors (λ) are set to unity. The variances of the innovations terms (ζ) are estimated. A measurement error term also influences the variance of each observed variable and is equated across twins and in our model for the first three measurements. The β weights are solely responsible for the covariation among variables. Correlations between co-twins for additive genetic factors (A) are fixed to one for MZ twin pairs and .5 for DZ twin pairs. Correlations for shared environmental factors (C) are one for both MZ and DZ twin pairs. Non-shared environmental factors (E) are uncorrelated between co-twins.

(Boomsma & Molenaar, 1987). Figure 1 represents the simplex model.

It includes causal pathways or transmission effects (β) between genetic (A) or environmental (C or E) latent factors that influence the trait at different occasions. As a result, genetic or environmental factors at a particular time-point are influenced by factors preceding that time-point. Furthermore, the model includes innovations (ζ). The innovation is that part of the latent factor that is not caused by a latent factor at a preceding occasion. At the first occasion the first latent factor cannot be explained by factors associated with an earlier point in time, and therefore this factor itself is regarded as an innovation (van Beijsterveldt et al., 2003). In a genetic study, the genetic innovations represent the expression of a new set of genes.

The simplex model can distinguish the nonshared environmental variance in measurement error (ε) and 'real' nonshared environmental innovations (ζe). There is an important distinction between innovations of latent variables and measurement errors of observed variables. The innovations are the part of the

latent variable at time i that is not caused by the latent variable at time i-1, but are part of every subsequent observed variable, i + 1, i + 2, and so on. In contrast, the random errors of measurement do not influence subsequent observed variables (Cornes et al., 2007).

λ in Figure 1 represents the loadings of the observed phenotype on the latent factors. These loadings were set to unity, so that the scaling of the latent factors is identical to the scaling of the phenotype. Because at occasion 4, a different instrument was used, the variance of measurement errors could not constrained to be equal across all time points. We constrained the first 3 measurement error variances to be equal and constrained the measurement error variance at occasion 4 at zero. This means that for time-point 4, the measurement error is included in the E innovation at time-point 4. To test the fit of the simplex model, a Cholesky model was used as reference model (Neale & Cardon, 1992). The Cholesky decomposition is descriptive and not driven by a specific developmental hypothesis. The model is a saturated unconstrained model which decomposes a

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Table 1

Number of Complete and Incomplete Twin Pairs, Age of Twins, Means and Variances of YASR-OCS (1991, 1995 and 1997) and PI-R ABBR (2002)

	Number of complete and incomplete twin pairs								Age (SD)				Mean (Variance)			
	1991		1995		1997		2002		1991	1995	1997	2002	1991	1995	1997	2002
	Com	Inc	Com	Inc	Com	Inc	Com	Inc								
MZM	273	0	272	10	216	76	236	181	17.6 (2.3)	19.7 (3.1)	25.4 (9.9)	32.8 (11.9)	2.2 (4.2)	1.8 (3.9)	1.8 (3.7)	7.9 (32.8)
DZM	231	11	223	6	147	64	99	151	17.6 (2.2)	19.8 (3.1)	25.2 (9.6)	33.1 (11.5)	2.4 (4.9)	2.2 (4.6)	2.1 (4.8)	7.6 (30.4)
MZF	380	3	422	15	407	120	631	342	17.6 (2.1)	19.6 (3.1)	26.4 (10.5)	33.5 (11.7)	2.7 (5.6)	2.7 (5.4)	2.6 (5.5)	8.2 (33.1)
DZF	280	3	258	16	244	107	293	251	17.8 (2.4)	20.0 (3.2)	26.0 (10.0)	32.9 (11.0)	3.0 (6.5)	2.6 (6.1)	2.6 (5.6)	7.8 (27.8)
DOS-M	473	6	453	36	318	166	290	383	17.8 (2.2)	20.0 (3.2)	24.3 (8.9)	31.2 (9.9)	2.5 (8.3)	2.3 (5.0)	2.0 (4.1)	8.3 (28.1)
DOS-F													2.9 (5.5)	2.6 (5.2)	2.5 (5.3)	8.2 (30.5)

Note: MZM, monozygotic males; MZF, monozygotic females; DZM, dizygotic males; DZF, dizygotic females; DOS-M, male half of a complete dizygotic opposite sex pair; DOS-F, female half of complete dizygotic opposite sex pair; Com, complete twin pair; Inc, incomplete twin pair; SD, standard deviation.

covariance matrix into genetic and non-genetic covariance matrices and thus is a first approach to obtain genetic and environmental correlations across time in longitudinal datasets.

Results

Sample Characteristic and Descriptive Statistics

Table 1 also gives an overview of means and variances.

No significant differences in means and variances over zygosity were seen at all 4 time-points, except at time-point 1995 (χ^2 = 8.74, df =2, p <.01). At that time-point DZ men scored higher on the ASR-OCS than MZ men. Significant sex-differences were seen in 1991, 1995 and 1997 with women scoring higher than men (all p < .01). In 2002, women seemed to score higher on the PI-R ABBR, but this was nonsignificant (χ^2 = 2.78, df =1, p = .10). The same pattern is also seen for the variances; significant variance differences between men and women on the first three time-points (all p < .01) and a nonsignificant difference on the last time-point (χ^2 = 0.49, df = 1, p = .48).

Table 2, first part, shows the within-person phenotypic correlations over time for men and women.

OC behavior was moderately to highly stable with correlations across time between r = .2 (for 11-year intervals), .4 (for 4- to 5-year intervals) and .6 (for 2-year intervals). The correlations between the YASR-OCS in 1997 and PI-R ABBR in 2002 were essentially the same (.39 for men and .40 for women) as between the YASR-OCS in 1991 and 1995 (.41 for men and .48 for women), both intervals covering about the same time interval.

The summary of twin correlations at each time-point and of the cross-twin–cross-time-point correlations is shown in Table 3.

The twin correlations within time-points show that MZ correlations are generally higher than DZ correlations. This suggests that both genes and non-shared environmental influence explain individual differences in OC symptoms. Only in 2002 in men, the DZ correlation is close to the MZ correlation, suggesting the influence of shared environment at

that time-point. Cross-twin–cross-time-point correlations represent the correlations between the OC symptom score at one time-point (e.g., 1991) in one twin, with the OC symptom scores of another time-point for another twin. As can be seen, for almost all cross-correlations, the MZ correlations are higher than DZ correlations, indicating the influence of genes on the covariance of OC symptoms across time.

Genetic Analyses

The simplex ACE model fitted very well against the Cholesky model (χ^2 = 6.9, df = 16, p = .98). As expected from the twin correlations, the AE simplex model with sex differences described the data well (χ^2 =

Table 2

Within Person Correlations Over Time (a) and Correlations Among Additive Genetic and Non-Shared Environmental Factors Between Different Time-Points (b)

	Within person correlations over time (a)			
	1991	1995	1997	2002
1991	1	.48	.42	.25
1995	.41	1	.61	.32
1997	.35	.52	1	.40
2002	.16	.28	.39	1

Correlations among additive genetic and nonshared environmental factors between different time-points (b)

	Additive genetic architecture			
	1991	1995	1997	2002
1991	1.00	.90	.80	.49
1995	.76	1.00	.89	.54
1997	.63	.82	1.00	.61
2002	.39	.52	.63	1.00

	Nonshared environment architecture			
	1991	1995	1997	2002
1991	1.00	.17	.12	.05
1995	.20	1.00	.34	.15
1997	.12	.32	1.00	.22
2002	.05	.15	.21	1.00

Note: Correlations for men and women are reported below and above diagonal, respectively.

Table 3

Twin Correlations for YASR-OCS (1991, 1995 and 1997) and PI-R ABBR (2002) and Cross-Twin–Cross-Time Correlations

	Cross-twin–within time correlations				Cross-twin–cross-time correlations					
zygosity	1991	1995	1997	2002	91–95	91–97	91–02	95–97	95–02	97–02
MZM	.41	.39	.46	.37	.30	.38	.23	.38	.22	.28
DZM	.10	.24	.11	.35	.05	.01	−.02	.31	−.05	.06
MZF	.35	.53	.47	.44	.33	.34	.18	.51	.25	.26
DZF	.25	.25	.32	.21	.30	.19	.18	.19	.08	.12
DOS	.17	.18	.19	.19	.18	.15	.17	.20	.16	.14

Note: MZM, monozygotic males; MZF, monozygotic females; DZM, dizygotic males; DZF, dizygotic females; DOS, dizygotic opposite sex.

12.8, $df = 14$, $p = .54$). To test whether the parameter estimates differed between men and women, the parameters of the AE model were constrained to be equal across sex. The fit of the model without sex differences deteriorated significantly ($\chi^2 = 54$, $df = 15$, $p = .00$), because of variance differences between men and women. This means that the AE simplex model with sex differences is the best fitting model. Figure 2 shows the unstandardized estimates of the AE model.

These estimates can be used to compute the relative contributions of A and E to the time-point specific total variances and stability coefficients. The genetic contribution to OC symptoms at each time-point consisted of genetic influences novel to that time-point (innovations), plus the genetic effects that were already operating at a previous time-point (transmission effect). The standardized innovation is obtained by dividing the squared innovation coefficient by the total variance. For example, the innovation effect at time-point 1997 for boys is $(.76^2)/4.21 = 14\%$. The percentage of the genetic variance at time-point 1997 that is transmitted from the previous time-point can be obtained by dividing the product of the squared transmission coefficient ($.84^2$) and the genetic variance of the previous time-point ($1.36^2 \times .74^2 + .86^2 = 1.75$) by the total variance:
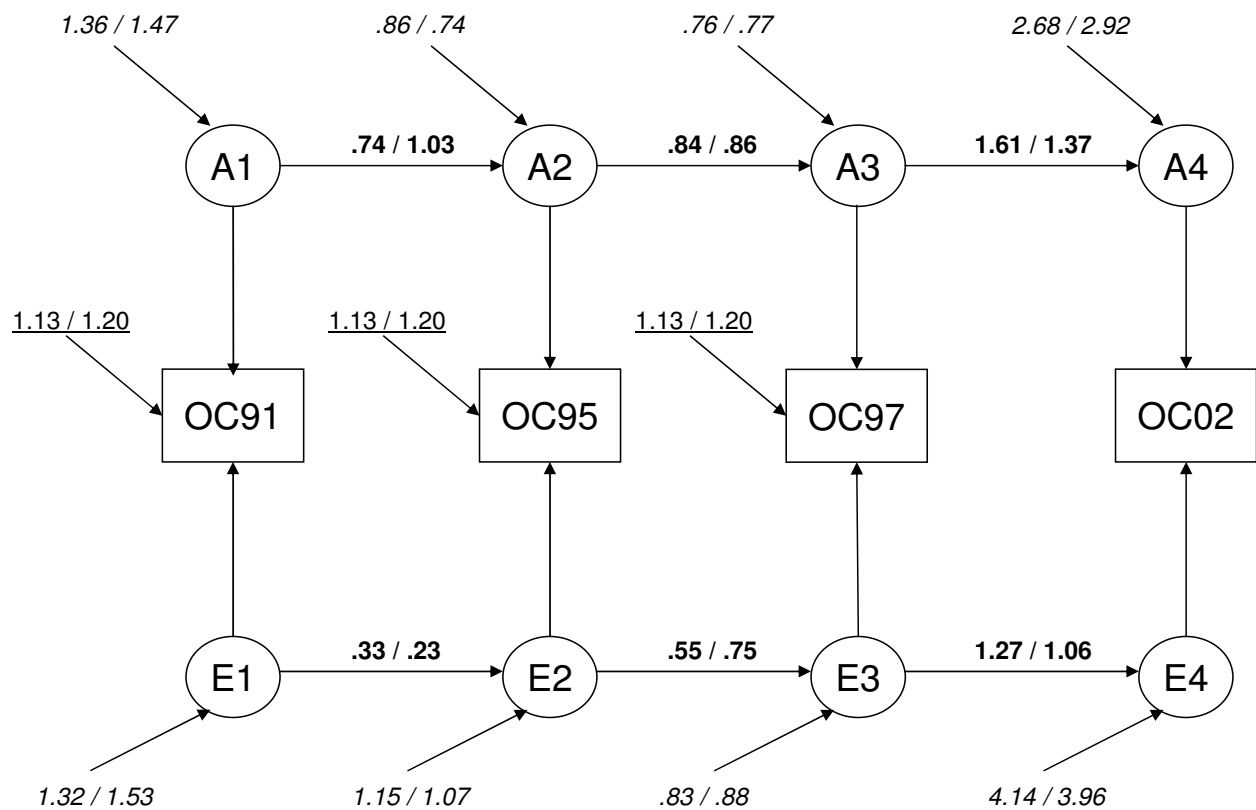
Figure 2

Unstandardized estimates of the final simplex model for OC symptoms at four time-point for men (left) and women (right). The squares represent the observed variance for each time-point (OC91, OC95, OC97 and OC02). The circles represent the latent factors. A = genetic influences, E = nonshared influences. We distinguish innovation effects (italics), transmission effects (bold) and measurement error (underscore).

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Table 4

Relative Contributions of Additive Genetic and Non-Shared Environmental Components to the Total Variances (Diagonal) and Covariances (Off-Diagonal) for YASR-OCS (1991, 1995 and 1997) and PI-R ABBR (2002) in Men and Women

Men	Additive genetic architecture (A)				Nonshared environment architecture (E)			
	1991	1995	1997	2002	1991	1995	1997	2002
1991	.38				.62 (*.36* + 26)			
1995	.70	.39 (**.22** + *.17*)			.30	.61 (**.04** + *.29* + .28)		
1997	.78	.64	.43 (**.29** + *.14*)		.22	.36	.57 (**.10** + *.17* + .30)	
2002	.82	.69	.67	.38 (**.15** + *.23*)	.18	.31	.33	.62 (**.06** + *.56*)
Women								
1991	.36				.64 (*.40* + 24)			
1995	.81	.51 (**.41** + *.10*)			.19	.49 (**.02** + *.21* + .26)		
1997	.83	.72	.47 (**.37** + *.10*)		.17	.28	.53 (**.13** + *.14* + .26)	
2002	.86	.77	.70	.44 (**.16** + *.28*)	.14	.23	.30	.56 (**.05** + *.51*)

Note: On the diagonals, the genetic influences are partitioned into transmission effects (bold) and innovation effects (italics). The nonshared influences are partitioned into transmission effects (bold), innovation effects (italics) and measurement error (underscore).

$(.84^2) \times 1.75/4.21 = 29\%$. This means that 43% (14% + 29%) of the total variation in OC symptoms is caused by genetic factors. An overview of the relative contribution of A and E for each time-point is given on the diagonal of the first part of table 4 for men (top part) and women (lower part).

At each age the contribution of genetic factors was substantial and remained quite stable across time-points and appears independent from the questionnaire used. Averaged over time-points, 40% (for men) and 45% (for women) of the variance was explained by genetic factors. The contribution of time-point specific genetic factors differed across time-points and across sex.

For nonshared environmental variance the transmission was low and varied between 2% and 13%. Most nonshared environmental variance consisted of time-point specific variance. Measurement error explains roughly 25% of the total variance at the first 3 time-points. For time-point 4 the measurement error was included in the total non-shared environmental variance.

About 70% to 80% of the stability in adulthood is a result of additive genetic effects. This can be seen in table 4, where the off-diagonal elements show the decomposition of the phenotype stability across time. The contributions of nonshared environmental factors to the stability were small.

Finally, the correlations in Table 2, second part, indicate the degree of overlap between genetic and environmental influences at one age and influences at subsequent time-points. The additive genetic correlations are between .63 and .82 for men across the first three time-points and between .39 and .63 between the first three time-points and the last time-point. For women, the correlations varied between .80 and .90 between the first three time-points, and .49 and .61 for the last time-point.

Discussion

We examined genetic and environmental contributions to stability over time of OC symptoms in adults. We found that OC symptoms are moderately stable across time and that, in contrast to the modest longitudinal phenotypic correlations, the longitudinal genetic correlations were high. We observed genetic correlations between roughly .4 (for 11-year periods) and .9 (over 2- to 4-year periods). Therefore, the main reason for stability of OC symptoms in adults was that the genetic influences on OC symptoms are stable across time, that is, to a large extent the same genes are expressed across time.

The moderate phenotypic stability seems in line with the clinical studies, which presented a more optimistic view of the course of OCD (Angst et al., 2004; Orloff et al., 1994; Reddy et al., 2005; Skoog & Skoog, 1999; Steketee et al., 1999). These studies suggested a relatively favourable course and outcome of OCD that is otherwise considered to be a chronic illness with waxing and waning course. Our results support the notion that having OC symptoms at one age does not automatically imply having OC symptoms for the rest of one's life.

Interestingly, in our paper examining stability for OCS in children (van Grootheest et al., 2007a), we came to the same conclusion, although one difference appeared between the two studies. In adults, genetic factors explained 70% of the stability, in children this was 40%. In children, part of the stability was due to common environmental factors shared by children growing up in the same household. These influences are not seen in adult twins, who generally do not live together with their cotwin when they are adults. Thus, phenotypic stability is roughly the same in children and adults, but the causes of stability differ. We also found that there is little transmission of unique environmental factors, implying that, on a population

level, individual experiences have limited impact on the stability of OC symptoms in adults.

We found sex-differences in average OC symptom scores at three time-points, but not at the last time-point. In 2002, the PI-R ABBR, instead of the YASR-OCS was used. Therefore, the diminishing sex differences in OC-symptoms scores could be caused by the use of a different measurement, although the possibility that the sex differences are age-dependent cannot be excluded. As longitudinal prevalence studies are scarce, we cannot compare these results with other studies. However, the results are in line with several studies which found no sex-differences or at the most a slight preponderance for women having OCD (Crino et al., 2005; Nestadt et al., 1998; Torres et al., 2006).

With the simplex model the variance associated with measurement error was estimated. Around 25% of the total variation of OC symptoms was accounted for by measurement error. Thus, 75% of the variation is 'true' variance due to genetic and environmental effects and after correcting for measurement errors, genetic factors account for more than 50% of this variation.

Even more important is the finding that in general the same genes account for OC symptoms at different ages. Also the proportion of variance explained by genetic factors is remarkably similar in both sexes. Taking into account earlier research, where we concluded that the same genes accounted for OC symptoms in men and women (van Grootheest et al., 2007b) plus the existence of stable genetic factors, it would imply that data of men and women at different ages can be pooled together in molecular genetic research projects, obtaining an increase of power.

The results of this study should be interpreted in the context of some potential limitations. Firstly, although both the YASR-OCS and PI-R ABBR show moderately high sensitivity and specificity in diagnosing DSM-IV OCD, the genetic and environmental contributions presented in this report reflect OCS scores, not clinical measures of DSM-IV OCD. Because of the relatively low prevalence of OCD, twin studies rely on dimensional measures with the underlying assumption that OCD reflects the end of a normal distribution, while OC symptoms represent a milder form of the latter (Jonnal et al., 2000; Kendler, 2005; van den Oord et al., 2003).

Second, the YASR-OCS and PI-R ABBR were used in a longitudinal design without knowledge about the relationship between the two instruments cross-sectionally. However, as the heritability estimates at different time-points are similar and genetic correlations are moderate, we expect that both questionnaires are measuring mainly the same genetic liability to OCS.

Third, both the YASR-OCS and PI-R ABBR showed a skewed distribution. One could use a threshold model to deal with this problem, but the disadvantage of a threshold model is the loss of power (Derks et al., 2004). Therefore, we used continuous scales with the

disadvantage of possibly underestimating the twin and longitudinal correlations, resulting in underestimating the genetic contributions to OCS.

Fourth, the use of twin models requires several assumptions, including the absence of assortative mating, the equal environment assumption, and the absence of gene-environment interaction and correlation. Van Grootheest et al. (van Grootheest et al., 2008) found small, but significant assortative mating for OC symptoms but concluded that the bias in twin studies caused by the small amount of assortment is negligible. Jonnal et al. (2000) tested the EEA for OC symptoms and concluded that the EEA was not violated. Gene–environment interaction could affect twin similarity in either direction depending on whether both twins are exposed to the specific environmental factor in question; to our knowledge, gene–environment interaction and/or correlation have yet to be demonstrated for the phenotype studied here.

In summary, this study provides evidence from a large sample of twins that OC symptoms are moderately stable over time and this stability is strongly influenced by additive genetic factors. We did find high to moderate genetic correlations over time, suggesting that in general the same genes influence OC symptoms over time.

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Declarations of Interest

None.

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