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Genetic and environmental influences on obsessive-compulsive symptoms in adults: a population-based twin-family study

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ABSTRACT

Background. The contribution of genetic factors to obsessive-compulsive (OC) symptoms has not been examined using a large population-based sample of adults. Furthermore, the extent to which there are qualitative and quantitative differences in genetic architecture between men and women with OC symptoms has not been elucidated.

Method. We obtained the Young Adult Self Report Obsessive-Compulsive Scale (YASR-OCS) from a group of 5893 monozygotic (MZ) and dizygotic (DZ) twins, and 1304 additional siblings from the population-based Netherlands Twin Register. Structural equation modelling was used to decompose the variation in OC behaviour into genetic and environmental components and analyse quantitative and qualitative sex differences.

Results. Familial resemblance was the same for DZ twins and non-twin siblings, which means that there was no evidence for a special twin environment. The same genetic risk factors for OC behaviour were expressed in men and women. Depending on the choice of fit index, we found small (39% for men and 50% for women) or no sex differences (47% for both men and women) in heritability. The remaining variance in liability was due to individual-specific environment.

Conclusions. OC behaviour showed a moderate heritability. At most, small quantitative sex differences were found in the genetic architecture of OC behaviour, and no qualitative sex differences.

INTRODUCTION

Historically, family-genetic studies have strongly suggested genetic factors to be important in the development of obsessive-compulsive disorder (OCD) (Black *et al.* 1992; Pauls *et al.* 1995; Nestadt *et al.* 2000*b*). For the determination of the relative importance of genetic and environmental factors, twin studies are an obvious choice. Twin studies of OCD have a long history, starting back in 1929 (Lange) and evolving from single case reports to large epidemiological studies (van Grootheest *et al.* 2005). A paper by Clifford *et al.* (1984) marked the beginning of research on quantitative OC traits in relatively large twin samples from the normal population, measuring OCD with standardized instruments. Clifford *et al.* (1984) analysed the 42-item version of the Leyton Obsessional Inventory (Cooper, 1970), obtained in 419 adult male and female twin pairs. The heritability of the obsessive symptoms was estimated at 47%. Since then, only one twin study on OC symptoms in adults has been published. Jonnal *et al.* (2000) examined data from 527 pairs of female monozygotic (MZ) and dizygotic (DZ) twins from the Virginia Twin Registry, using 20 items of the Padua Inventory (PI; Sanavio, 1988). The best model for these data suggested heritabilities of 33% and 26%

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for obsessiveness and compulsiveness respectively.

In children, a large twin study on OC behaviour, assessed by the Child Behavior Checklist Obsessive-Compulsive Scale (CBCL-OCS), was conducted in an American and Dutch twin sample (Hudziak *et al*. 2004). OC behaviour was assessed at ages 7, 10 and 12 years and showed a heritability of approximately 55%. Significant sex differences in heritabilities were only seen in the US sample. Van Grootheest *et al*. (2007) found that stability of OC behaviour in children, using the CBCL-OCS at ages 7, 10 and 12 years in a longitudinal design, was influenced by genes and both shared and non-shared environmental factors. Bolton *et al*. (2007) examined 6-year-old twins on OC symptoms; the effect of familial aggregation was estimated as 47% for subthreshold OCD, but the study missed power to distinguish shared environment from genetic factors.

In summary, twin studies are suggestive of genes being important for variation in OC behaviour in children. For adults, a large twin study in males and females using a biometrical approach with continuous data is needed to provide more conclusive evidence and explore additional questions (van Grootheest *et al*. 2005). In particular, the impact of sex on the transmission of OCD in adults is unknown. Sex effects can be either quantitative (i.e. sex differences in magnitude of heritability) or qualitative in nature (i.e. whether the genetic risk factors for OC symptoms in men and women are the same). Knowledge about sex effects in genetic risk for OCD is important because some literature on sex differences in OCD, although not always consistent, exists. Clinical studies of OCD have shown that males are more likely to have a childhood onset, have a more chronic course of disease, and show OC symptoms that are associated with a distinct pattern of co-morbid psychopathology (Geller *et al*. 1998; Eichstedt & Arnold, 2001). Several association studies have produced variable evidence for association in one sex or another (Camarena *et al*. 2001; Enoch *et al*. 2001; Alsobrook *et al*. 2002; Lochner *et al*. 2004; Hemmings & Stein, 2006). Segregation analyses suggest that the inheritance of OCD could be affected by sex effects (Nestadt *et al*. 2000*a*; Hanna *et al*. 2005).

The aim of this study was to determine the genetic and environmental contributions to OC symptoms in adults by using a large sample of unselected twins and siblings. To maximize the statistical power and to test whether the results generalize to non-twins, the classical twin design was extended by including siblings (Posthuma & Boomsma, 2000; Stoel *et al*. 2006). OC symptoms were assessed using the adult version of the CBCL-OCS, the Young Adult Self Report Obsessive Compulsive Scale (YASR-OCS). The criterion validity of the YASR-OCS was tested with receiver operating characteristic (ROC) analyses among three different groups: an OCD group, a psychiatric control group and a population control group. We sought answers to the following questions:

(1) What are the psychometric properties of the YASR-OCS?
(2) Can results from our study be generalized to non-twins?
(3) What role do genetic and environmental factors play in the aetiology of OC symptoms?
(4) Are genetic and environmental risk factors for OC symptoms of similar importance in males and females?
(5) Are the genetic risk factors for OC symptoms in men the same as in women?

METHOD

Subjects

This study is part of a longitudinal survey study in twin families registered with the Netherlands Twin Register (Boomsma *et al*. 2002, 2006). Since 1991, every 2 to 3 years twins and their families have received a survey by mail containing questionnaires about health, personality and lifestyle. Participants in this study were adolescent and adult twins (mean age 22·4 years, S.D. = 8·3) and their siblings (mean age 28·0 years, S.D = 11·0). Data were available for twins who participated in surveys in 1991, 1995 and 1997 and for siblings who participated in the survey of 1997. The data from these three surveys were used to create a large cross-sectional data set. We added, when possible, two additional sibs to each twin family. First, data for twin pairs and their siblings from the 1997 survey were used. If no twin data were available

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Table 1. *Number of families per zygosity in the study with the number of twins and siblings per family*

		One sibling		Two siblings		
	No siblings	Male	Female	Male/male	Female/female	Male/female
MZM families						
Two twins	305	60	56	7	10	24
One twin	26	4	8	0	1	2
MZF families						
Two twins	487	83	105	19	18	29
One twin	37	3	5	0	2	3
DZM families						
Two twins	246	50	51	4	10	16
One twin	27	3	3	0	1	2
DZF families						
Two twins	324	64	62	6	18	11
One twin	38	1	9	1	3	3
DOS families						
Two twins	488	99	108	11	21	32
One twin	46	2	10	1	2	2

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

in 1997, then data for twin pairs collected in 1995 or 1991 were used. Half sibs, adoptive sibs and triplets were excluded. The resulting sample consisted of 5893 twins: 3360 females and 2533 males from 3069 families. We were able to include 1304 additional non-twin siblings, 713 sisters and 591 brothers. A non-twin sibling can form a (twin-)sibling pair with one twin brother or sister, and a (twin-)sibling pair with their other twin brother or sister. In the case of two siblings, the siblings form a sibling pair by themselves. These non-twin siblings increased the number of sibling pairs to 2773. As a consequence of the inclusion of additional siblings, the MZ-pair to DZ-pair ratio decreased from 0·75 (792/1058) to 0·21 (792/3831). It has been shown that an MZ to DZ ratio of about 1 to 4 is optimal in terms of statistical power (Nance & Neale, 1989). Table 1 provides information on the twin/sibling composition and sex distribution of the participating families for each zygosity group. 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, information on their zygosity was available from DNA polymorphisms. The agreement between zygosity diagnoses of the questionnaire and DNA data was 98% (Willemsen *et al.* 2005).

ROC analyses were conducted among three different groups: an OCD group, a psychiatric control group and a population control group. Data on patients with OCD were derived from the out-patient anxiety clinic of GGZ Buitenamstel, a specialized centre for anxiety disorders in Amsterdam. All participants who presented themselves for diagnosis and/or treatment of OCD between August 2004 and September 2005 were invited for a longitudinal study of OCD. In total, 68 participants, 22 men and 46 women with a mean age of 36·8 (S.D = 10·2), were diagnosed by trained psychiatric residents using the Structured Clinical Interview of DSM-IV (SCID-I; First *et al.* 1996). A group of 66 psychiatric control participants without OCD, consisting of 16 men and 50 women with a mean age of 36·6 (S.D = 9·8), was obtained from an adult sample of the Netherlands Twin-family Study on Anxious Depression (NETSAD; Boomsma *et al.* 2000). Psychiatric diagnoses of the participants were obtained in 1997 by telephone interviews using the Composite International Diagnostic Interview (CIDI; WHO, 1992). For a detailed description of the data collection, see Boomsma *et al.* (2000) and Middeldorp *et al.* (2006). Data were used from participants with actual diagnoses within the past 12 months. The index diagnoses of the psychiatric control group participants varied from depression, panic disorder and social phobia to general anxiety disorder. The population control group was obtained from the NETSAD and was selected

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Table 2. *YASR items used for the YASR-OCS*

YASR item no.	YASR item	YASR syndrome on which item is scored
9	I cannot get my mind off certain thoughts	Thought problems
31	I am afraid I might think or do something bad	Anxious/depressed
32	I feel I have to be perfect	Anxious/depressed
52	I feel too guilty	Anxious/depressed
66	I repeat certain acts over and over	Thought problems
84	I do things other people think are strange	Thought problems
85	I have thoughts that other people would think are strange	Thought problems
112	I worry a lot	Anxious/depressed

YASR-OCS, Young Adult Self Report Obsessive-Compulsive Scale.

for absence of any diagnosis. The 68 participants were selected to match OCD participants in terms of age and sex.

Measures

The YASR is a standardized self-report questionnaire for adolescents and adults (Achenbach, 1997). It is derived from the CBCL, a parent-derived rating instrument for children aged between 4 and 18 years (Achenbach, 1991, 1997). The YASR has roughly the same format as the CBCL, except that items pertaining to childhood problems were replaced by items pertaining to adults' functioning. The YASR comprises 110 problem items, covering emotional and behavioural problems during the previous 6 months. The participants respond on a three-point scale with the code of 0 for not true, 1 for somewhat or sometimes true and 2 for very true or often true. Good reliability and validity of the YASR has been reported by Achenbach *et al.* (1987) and was supported for the Dutch version (Wiznitzer *et al.* 1992; Ferdinand & Verhulst, 1995). The YASR-OCS contains the same eight items as the CBCL-OCS (Nelson *et al.* 2001), except that items are worded in the first person (Table 2). Using a cut-off of 5 on the CBCL-OCS, 91% of all DSM-determined OCD cases were identified in a clinical sample of children with reasonable specificity (67·2%) (Hudziak *et al.* 2006). The CBCL-OCS also showed good reliability and validity in several other samples (Geller *et al.* 2006; Storch *et al.* 2006). A numerical value for the YASR-OCS is obtained by adding the scores on the relevant eight items (0, 1 or 2 per item), thus limiting the scale to a range between 0 and 16.

Data analyses

Psychometric analyses

Internal consistency of the YASR-OCS was obtained by Cronbach's α coefficient. ROC analyses were conducted to determine the extent to which the YASR-OCS can accurately identify persons with OCD. ROC analysis uses the association between sensitivity [true positives/(true positives + false negatives)] and specificity [true negatives/(true negatives + false positives)] to derive an area under the curve (AUC), which indicates how well a measure distinguishes between case positive (i.e. the OCD group) and case negative (i.e. psychiatric controls or population controls) irrespective of the base rate. A value of 0·50 of the AUC indicates chance level and 1·0 indicates a perfect diagnostic tool. For detailed descriptions of the underlying principles of ROC analysis see Swets (1996) and McFall & Treat (1999). We also calculated positive and negative predictive values, respectively abbreviated as PPV [true positives/(true positives + false positives)] and NPV [true negatives/(true negatives + false negatives)]. ROC analyses were conducted with SPSS Version 12.0.1 (SPSS Inc., Chicago, IL, USA).

Genetic analyses

Genetic analyses include data from siblings in addition to MZ and DZ twins. This extension of the classical twin design provides increased statistical power, both for gene detection (Dolan *et al.* 1999) and for estimation of the genetic and common environmental influences (Posthuma & Boomsma, 2000; Stoel *et al.* 2006). Genetic analyses decompose the variance of the liability to OC symptoms into its genetic and environmental contributions. We assumed that twin resemblance arises from two latent factors, additive genetic factors (A) and shared environmental factors (C). MZ twins share all of their genes, whereas DZ twins and non-twin siblings share on average 50% of their segregating genes. Any familial resemblance due to genetic additive factors will therefore be higher for MZ twins than for DZ twins and non-twin siblings.

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Shared environmental factors, experiences shared by members of a twin pair that tend to make them similar, contribute equally to the correlation in MZ and DZ twins. In addition to A and C, the model includes non-shared or individual-specific environment (E), which reflects measurement error and individual experiences that make members of a twin pair different in their liability to OC symptoms.

Because the data exhibited a pronounced right skew, we used a threshold model under the assumption of an underlying continuous liability distribution with the thresholds defining categories (Derks *et al*. 2004). The thresholds are chosen in such a way that the prevalences are more or less similar in each of the categories. We used three thresholds because the use of more thresholds had the disadvantage of the presence of empty cells. To correct for multiple testing, we tested each model in the sequence at a significance level (α) of 0·01. Genetic analyses were carried out in several steps using the software package Mx (Neale *et al*. 2003).

We first fitted a saturated model in which thresholds and polychoric correlations between twin pairs, twin-sibling pairs and sibling-sibling pairs were estimated without any restrictions. In model-fitting procedures, the saturated model is used as a starting-point for the comparison of different, nested models. The fit and parsimony of the various nested models are judged using likelihood ratio tests in which the negative log-likelihood (-2LL) of the nested model is compared with -2LL of the saturated model. Subtracting the two -2LLs from each other yields a statistic that is asymptotically distributed as χ^2 with degrees of freedom (df) equal to the difference between the number of parameters in the two models. According to the principle of parsimony, models with fewer parameters are preferred if they do not give a significant deterioration of the fit. In addition, the Akaike Information Criterion (AIC), a goodness-of-fit index that considers the rule of parsimony, was calculated.

The comparison of MZ twin pair correlations with DZ twin pair and sibling pair correlations provides a first estimate of the sources of variation in individual differences in OC symptoms. Furthermore, to test whether a specific twin factor influences individual differences in OCS, we tested for heterogeneity of correlations between DZ twins and siblings. If DZ correlations are not equal to sib-sib correlations or twin-sib correlations, it indicates the existence of a special twin environment.

Next, a threshold model was used to partition the variance of the underlying liability for OC symptoms into additive genetic (A), shared environmental (C) and non-shared or individual-specific environment (E). Analysing all zygosity groups (i.e. male MZ twin pairs and DZ twin/sib pairs, female MZ twin pairs and DZ twin/sib pairs, DZ opposite-sex twin/sib pairs) enabled us to examine two different sex effects. The magnitude of the genetic and environmental influences was constrained to be equal for men and women to test if the importance of the genetic and environmental factors is similar for men and women. By constraining the genetic correlation for opposite-sex pairs to 0·5, an explicit test was conducted to determine whether the same genetic factors operate in males and females.

RESULTS

Psychometric analyses

ROC analyses showed an AUC of 0·84 [95% confidence interval (CI) 0·78–0·91] on the YASR-OCS when compared to clinical controls. When compared to general population controls, the AUC was 0·95 (95% CI 0·92–0·99). At the best cut-off point of 7, the sensitivity was 82·4% and the specificity was 69·7% when compared to clinical controls. The PPV and NPV were 73·7% and 79·3% respectively. Cronbach's α coefficient for the eight items of the YASR-OCS was 0·69.

Genetic analyses

All thresholds for OC symptoms could be constrained to be equal for both twins in pairs [$\chi^2(12) = 7{\cdot}34$, $p = 0{\cdot}83$], in same-sex and opposite-sex DZ pairs [$\chi^2(18) = 20{\cdot}0$, $p = 0{\cdot}33$], in MZ and DZ same-sex pairs [$\chi^2(30) = 38{\cdot}3$, $p = 0{\cdot}14$], and sibs and twins [$\chi^2(36) = 43{\cdot}8$, $p = 0{\cdot}17$]. Thresholds for men and women were different [$\chi^2(33) = 261{\cdot}7$, $p \leqslant 0{\cdot}001$], with lower thresholds for women than men, indicating a higher prevalence in women in OC behaviour.

Table 3 displays the correlations of the five different zygosity groups. The siblings are included in the DZ groups, because a comparison

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Table 3. *Twin correlations on YASR-OCS scores by zygosity*

MZM	MZF	DZM/sibsMM	DZF/sibsFF	DOS/sibsOS
0·44	0·50	0·13	0·26	0·21

YASR-OCS, Young Adult Self Report Obsessive-Compulsive Scale; MZM, monozygotic males; MZF, monozygotic females; DZM, dizygotic males; DZF, dizygotic females; DOS, dizygotic opposite sex; sibsMM, brothers; sibsFF, sisters; sibsOS, sibs of opposite sex.

with the fully saturated model revealed that all sibling correlations could be constrained to be equal to the DZ correlations for males and females [$\chi^2(70) = 89{\cdot}3$, $p = 0{\cdot}16$], showing that there was no specific twin environment. The MZ correlations are substantially higher than the DZ correlations for both men and women, suggesting that shared environmental effects do not contribute to individual differences in OC behaviour. For both males and females, MZ twin correlations are clearly different from unity, indicating non-shared environmental effects on the YASR-OCS.

The results of genetic model fitting are summarized in Table 4. The ACE model (model 2) describes the data adequately when compared with the fully saturated model (model 1). Next, a model was fitted without the shared environmental effect (model 3). The fit did not get significantly worse. In model 4 we constrained the correlation of the genetic factors for opposite-sex twins to be 0·5. This did not give a significant deterioration in fit, which suggests that the same genes account for variation in OC behaviour in men and women. In model 5 we constrained the magnitude of the effect of the genetic risk factors to be the same in men and women. This model just fits the data, suggesting no differences in heritability between men and women. However, according to the AIC, model 4 has a lower AIC value in comparison to model 5. Therefore, according to the AIC, model 4 would be the model of choice. The AIC adjusts χ^2 for the number of estimated parameters and can sometimes give a different result than a likelihood ratio test.

Model 4 estimated the heritability of OC behaviour to be 39% for men and 50% for women. Model 5 estimated the heritability of OC behaviour to be 47% for both men and women. The remaining variance in liability for OC symptoms was attributed to non-shared environment.

DISCUSSION

This is the first adult twin-family study to investigate sex effects in the influence of genetic and environmental factors on individual differences in OC behaviour in a large population-based sample of twins and sibs. Five major conclusions can be drawn. First, the YASR-OCS appears to be an effective instrument to screen for OCD in adults. Second, MZ and DZ twins did not differ from their siblings for prevalence of OC symptoms and DZ twins did not differ from their siblings for resemblance of OC symptoms, so the results of our study generalize to non-twins. Third, we found a modest heritability of individual differences in OC behaviour. Individual specific environment accounted for the remaining variance in OC behaviour. Fourth, depending on the fit index, the results suggest that there are small or no sex differences in the importance of genetic and environmental influences between men and women. Fifth, because the genetic correlation for opposite sex pairs could be constrained to 0·5, the genes that account for the genetic influence seem to be the same in both sexes.

Psychometric analyses

The YASR-OCS showed satisfactory psychometric properties with a sensitivity and specificity of 82% and 70% respectively. These findings are comparable with the performance of the CBCL-OCS, which demonstrated a sensitivity and specificity of 92% and 67% respectively in children. A major advantage of these two instruments is that they provide investigators and clinicians with two fully comparable screens on OC symptomatology along the lifespan. Determining the course and stability over time of OC behaviour, with a follow-up period covering childhood, adolescence and also adulthood, using age-adjusted instruments, has advantages over instruments developed for only one age period (Wiznitzer *et al.* 1992). The YASR-OCS is an instrument that seems to deal effectively with the discontinuity in available diagnostic and research tools between children and adolescents on the one hand and adults on the other.

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Table 4. *Model fitting results for heritability of YASR-OCS scores*

No. of model	Type of model[a]	−2LL	χ^2	df	p[b]	AIC	Compared with model
1	Fully saturated model	18477·0	—	—	—	—	—
2	ACE, quantitative and qualitative sex differences allowed	18630·7	153·7	121	0·02	4252·7	1
3	AE, quantitative and qualitative sex differences allowed	18630·9	0·2	2	0·90	4248·9	2
4	AE, quantitative sex-differences allowed, but no qualitative sex differences	18631·0	0·1	1	0·75	4247·0	3
5	AE, no quantitative and qualitative sex differences allowed	18636·0	5·0	1	0·03	4250·0	4

YASR-OCS, Young Adult Self Report Obsessive-Compulsive Subscale; LL, log-likelihood; df, degrees of freedom; AIC, Akaike Information Criterion.

[a] A, Additive genetic effects; C, common or shared environmental effects; E, non-shared or individual-specific effects. Quantitative sex differences = sex differences in magnitude of heritability. Qualitative sex differences = sex differences in genetic risk factors.

[b] Significance level (α) was set at 0·01.

Genetic analyses

Our results on genetic contribution are in line with those found by Clifford *et al.* (1984), but our heritability estimates are somewhat higher than estimates in women by Jonnal *et al.* (2000). Like Clifford *et al.* (1984) and Jonnal *et al.* (2000), we did not observe shared environmental influences on OC behaviour in adults. In children, a modest influence of shared environment has been found, especially at age 12 (Hudziak *et al.* 2004; van Grootheest *et al.* 2007). This finding might indicate a special period around adolescence for OC behaviour, when individuals are sensitive to the effects of the home environment. This is in line with a study by Geller *et al.* (2001) on developmental aspects of OCD in three groups: children, adolescents and adults. Specific clinical correlates and symptom profiles were associated with the disorder in different age groups and these findings supported a hypothesis of developmental discontinuity between juvenile and adult OCD.

In general, OC behaviour showed a moderate heritability in line with other internalizing phenotypes, such as general anxiety disorder (Hettema *et al.* 2001), panic disorder (Kendler *et al.* 2001) or depression (Kendler & Prescott, 1999). The heritabilities we found for adults are close, but lower, than the heritabilities of approximately 55% in the children sample of Hudziak *et al.* (2004). Obviously, the adult sample in this study included early-onset cases with OC symptomatology, in several studies associated with increased family history, as well as late-onset cases, associated with lower genetic load. The latter may temper the heritability in adults.

Our results suggest that there are small or no sex differences in heritability of OC behaviour, depending on the choice of fit index. This means that further research is needed before any firm conclusions can be drawn on the existence of quantitative sex differences. Hudziak *et al.* (2004) found no evidence for quantitative differences in children. In several family studies no gender differences were found in patients with a positive family history (Nestadt *et al.* 2000*b*; Chabane *et al.* 2005; Delorme *et al.* 2005). However, we found small sex differences in thresholds, with lower thresholds for women. This means that the prevalence for women is somewhat higher than for men, which seems to support earlier findings of a slight preponderance in the prevalence of OC symptoms in women (Nestadt *et al.* 1998; Crino *et al.* 2005; Torres *et al.* 2006).

The conclusion that, in general, the same genes may account for OC behaviour in men and women has implications for molecular genetic research. Our results emphasize the feasibility of treating OC behaviour as a quantitative trait to which a quantitative trait loci (QTL) approach can be applied, besides the approach of categorical analyses of clinical OCD cases (Miguel *et al.* 2005). Furthermore, these findings suggest that data of men and women can be pooled in molecular genetic analyses. This conclusion may seem in contrast to, for example, two recent association studies that found the glutamate transporter gene SLC1A1 to be associated with susceptibility to OCD, particularly in males (Arnold *et al.* 2006; Dickel *et al.* 2006). However, it should be noted that our results reflect the sum of all possible genetic effects associated with OC behaviour, which does not

rule out a small sex effect of a single candidate gene.

Limitations

The results of this study should be interpreted in the context of four potential methodological limitations. First, the modest number of items in the YASR-OCS may contribute to increased error variance. Second, the YASR-OCS is only specific to recent symptoms, not lifetime symptoms, as it measures symptoms of the past 6 months. Third, the genetic and environmental contributions presented in this report reflect YASR-OCS scores, not clinical measures of DSM-IV OCD. Although the YASR-OCS showed satisfactory criterion validity for DSM-IV OCD cases, we used the whole distribution of OC symptoms in the population 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; van den Oord *et al.* 2003; Kendler, 2005). A quantitative approach does justice to the fact that previous studies found high rates of subclinical OC symptoms in family members of OCD probands (Pauls *et al.* 1995; Nestadt *et al.* 2000*b*), which in a DSM-dichotomous approach would be missed (Miguel *et al.* 2005). As the YASR-OCS is developed as a short screening instrument, it was not possible to distinguish various symptom dimensions within OCD (Mataix-Cols *et al.* 2005). Fourth, the findings of this analysis are predicated on the assumptions of the method used. These assumptions include absence of assortative mating and the equal environment assumption (EEA). Maes *et al.* (1998) found that significant but moderate primary assortment exists for psychiatric disorders 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.

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DECLARATION OF INTEREST

None.

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