ORIGINAL ARTICLE

A Multivariate Twin Study of Obsessive-Compulsive Symptom Dimensions

Alessandra C. Iervolino, PhD; Fruhling V. Rijsdijk, PhD; Lynn Cherkas, DPhil; Miquel A. Fullana, PhD; David Mataix-Cols, PhD

Context: Obsessive-compulsive disorder (OCD) is clinically heterogeneous, but it is unclear whether this phenotypic heterogeneity reflects distinct, or partially distinct, etiologic mechanisms.

Objective: To clarify the structure of the genetic and environmental risk factors for the major symptom dimensions of OCD.

Design: Self-report questionnaires and multivariate twin model fitting.

Setting: General community.

Participants: A total of 4355 female members of the TwinsUK adult twin register.

Main Outcome Measures: Scores on the Obsessive-Compulsive Inventory–Revised and 5 of its subscales (checking, hoarding, obsessing, ordering, and washing).

Results: A common pathway model did not fit the data well, indicating that no single latent factor can explain the heterogeneity of OCD. The best-fit multivariate twin model was an independent pathway model, whereby both common and unique genetic and/or environmental factors contribute to the etiology of each symptom dimension. The hoarding dimension had the lowest loading on the common factor and was more influenced by specific genetic effects (54.5% specific). With the exception of hoarding, most of the genetic variance was due to shared genetic factors (ranging from 62.5% to 100%), whereas most of the nonshared environmental variance was due to dimension-specific factors.

Conclusions: Obsessive-compulsive disorder is unlikely to be an etiologically homogeneous condition. There is substantial etiologic overlap across the different OC symptom dimensions, but dimension-specific genetic, and particularly nonshared environmental, factors are at least as important. Hoarding shares the least amount of genetic liability with the remaining symptom dimensions. The results have implications for the current deliberations regarding OCD and the inclusion of a putative hoarding disorder in *DSM-5*.

Arch Gen Psychiatry. 2011;68(6):637-644

Author Affiliations: Departments of Psychosis Studies (Drs Iervolino, Fullana, and Mataix-Cols) and Psychology (Drs Iervolino and Mataix-Cols), MRC Social, Genetic and Developmental Psychiatry Centre (Dr Rijsdijk), King's College London, Institute of Psychiatry, Department of Twin Research and Genetic Epidemiology, King's College London School of Medicine (Dr Cherkas), London, England; and Anxiety Unit (IAPS [Institut d'Atenció Psiquiàtrica i Toxicomanies]–Hospital del Mar) and Department of Psychiatry, Autonomous University of Barcelona, Barcelona, Spain (Dr Fullana).

THE SYMPTOMS OF OBSESSIVE-compulsive disorder (OCD) are heterogeneous to the extent that 2 patients with this diagnosis can display different, nonoverlapping symptom profiles. At least 4 relatively independent symptom dimensions have been identified and widely replicated: (1) contamination/cleaning, (2) forbidden thoughts, (3) symmetry/order, and (4) hoarding.[1-3] Despite this phenotypic heterogeneity, the current classification systems (*DSM-IV* and *International Classification of Diseases, Tenth Revision*) regard OCD as a unitary entity. It has been suggested that this parsimony may be oversimplistic and could obscure the findings from studies attempting to understand the psychological and biological mechanisms implicated in OCD. More important, considering OCD as a unitary entity may hamper progress in developing new treatment strategies for this chronic, disabling condition.[1,2,4,5]

The phenotypic heterogeneity of OCD is unquestionable and some preliminary data support the validity of its major symptom dimensions[1,2,5]; however, it is unclear whether the observed heterogeneity reflects distinct or partially distinct etiologic mechanisms. Indeed, it is possible that a single etiologic mechanism or set of mechanisms can explain all symptoms of OCD. If this were correct, adopting a multidimensional approach may sidetrack researchers from the important common factors that may be involved in all types of OCD.[6] It is equally plausible that both common and unique etiologic mechanisms are implicated in the major symptom dimensions of OCD, as predicted by the multidimensional model.[1(p234)] If this were cor-

©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/25/2013

rect, some etiologic mechanisms may be common to all patients with OCD, whereas other mechanisms may be unique to each symptom dimension. Although some indirect evidence from family studies supports this hypothesis,[7] it remains to be fully tested.

Multivariate twin modeling methods are particularly well suited to test the assumptions of the multidimensional model. Specifically, these methods can be used to estimate the extent to which the covariation between different symptom dimensions is influenced by a single phenotypic latent factor (eg, OCD), which combines the contribution of common genetic and environmental factors, or whether each symptom dimension is better explained by genetic and environmental factors common to all symptom dimensions, as well as genetic and environmental factors specific to each. To date, only 2 small twin studies[8,9] have been conducted and have provided preliminary data suggesting that both common and specific genetic and environmental factors may contribute to the etiology of different obsessive-compulsive (OC) symptom dimensions. However, these studies have several methodologic shortcomings that limit their interpretation, primarily the use of instruments that lack coverage of the full range of OC symptoms, making them unsuitable for clarifying issues pertaining to the heterogeneity of OCD.

The main aim of the present study was to explore the extent to which covariation between the major OC symptom dimensions is explained by genetic and environmental factors in a large sample of female monozygotic (MZ) and dizygotic (DZ) twins (N=4355). Large epidemiologic samples of unselected twins from the general population offer an excellent means to examine the relative contribution of genetic and environmental factors to behavioral traits.[10] Based on the findings of previous family and twin studies (reviewed by van Grootheest et al[10]), we predicted that individual differences in the liability of broadly defined OCD would be influenced by genetic and nonshared environmental factors and that the influence of shared environmental factors would be negligible. Consistent with the multidimensional model of OCD, we predicted that there would be significant overlap or covariation between the different OC symptom dimensions and that these would be influenced by common as well as specific etiologic factors. Consistent with the current conceptualization of hoarding as a distinct dimension of OCD, or even a separate disorder,[11,12] we predicted that there would be a greater degree of specificity for hoarding symptoms.

METHODS

PARTICIPANTS

Participants were MZ and DZ twins from the TwinsUK adult twin registry (http://www.twinsuk.ac.uk). The sample characteristics have been described in detail elsewhere.[13] Briefly, the registry was started in 1993 and comprises nearly 10 000 white MZ and DZ twins, predominantly female for historical reasons, 16 years or older from throughout the United Kingdom. The twins have been shown[14] to be comparable to age-matched population singletons in terms of disease- and lifestyle-related characteristics. The Peas in the Pod questionnaire was used to ascertain zygosity,[15] which was confirmed in cases of uncertainty by DNA fingerprinting or genome-wide scans. All active twins in the registry (n=8313) were sent the Obsessive-Compulsive Inventory–Revised (OCI-R)[16] as part of a larger wave of data collection; 5022 twins returned this questionnaire. Responders and nonresponders were comparable in terms of zygosity (53% vs 50% MZ, respectively) and socioeconomic status[17] (mean [SD], 3.7 [1.2] vs 3.3 [1.3]). Nonresponders were more likely to be male (56% vs 36%; $\chi^2_1=189.9$; $P<.001$) and younger (46 [14] vs 55 [13] years; $t_{8312}=28.8$; $P<.001$). The sample available for analysis included 2053 twin pairs (125 MZ males, 65 DZ males, 971 MZ females, 857 DZ females, and 35 DZ twins of the opposite sex) and 916 singleton twins (73 MZ males, 56 DZ males, 383 MZ females, 316 DZ females, 34 DZ opposite-sex twins, and 54 DZ twins whose co-twin sex was unknown). More than 80% of the sample was female (4459 participants [88.8%]), and mean (SD) age was 55.5 (13.4) years (range, 17-86 years). All participants provided informed consent, and the study was approved by the St Thomas' Hospital Research Ethics Committee. The small number of male twins (n=509) and DZ opposite-sex twins (n=104) did not afford sufficient power to test quantitative and qualitative sex differences in the liability of the various OC symptom dimensions. For this reason, and to maximize homogeneity, twin analyses were performed using data only from same-sex female twins. Singleton twins for whom the co-twin sex was unknown (n=54) were also excluded, resulting in a final sample of 4355 for analysis.

MEASURES

The OCI-R[16] is a widely used 18-item self-report questionnaire designed to measure distress associated with OC symptoms. Each item is rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (extremely), with a total scale score ranging from 0 to 72. The OCI-R consists of six 3-item subscales with scores ranging from 0 to 12. These subscales broadly correspond to the major symptom dimensions of OCD[3] and are named *checking*, *hoarding*, *obsessing*, *ordering*, *neutralizing*, and *washing*. The OCI-R total and its subscales have excellent psychometric properties, including test-retest reliability, and convergent/discriminant validity.[16,18] Each of the OCI-R subscales correlates highly with the corresponding dimensions of the Dimensional Yale-Brown Obsessive Compulsive Scale,[19] the criterion standard in symptom dimension assessment.[20,21] A cutoff score of 21 on the OCI-R total scale discriminates between patients with vs those without OCD.[16] Scores higher than 3 on the washing and neutralizing subscales; higher than 5 on the checking, hoarding, and obsessing subscales; and higher than 7 on the ordering subscale discriminate patients with OCD who rate these symptoms as the most distressing from nonclinical controls, with sensitivity and specificity ranging from 0.83 to 1.00 and from 0.76 to 0.92, respectively.[22] These cutoff scores were used to establish meaningful thresholds for model fitting (see the "Data Analyses" subsection). In the current study, an exploratory principal components analysis, followed by promax rotation (SPSS 16.0; SPSS, Inc, Chicago, Illinois) revealed a 6-factor structure, which was identical to that reported in the original article by Foa et al[16] and explained 71% of the variance (eTable 1; http://www.archgenpsychiatry.com). It had good internal consistency for the total scale (Cronbach $\alpha=0.87$) and all of its subscales (checking, 0.83; hoarding, 0.80; obsessing, 0.82; ordering, 0.86; and washing, 0.77). An exception was the neutralizing subscale, for which internal consistency was only modest (0.54). For this reason, and because this subscale does not correspond to any of the established symptom dimensions of OCD, it was not included in the multivariate genetic analyses. However, its inclusion did not modify the overall results (data available upon request).

©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/25/2013

Table 1. Genetic Raw Ordinal Model-Fitting Analyses for the OCI-R Total Score for the Best-Fitting AE Model[a]

Model	–2LL	$\Delta\chi^2$	Δdf	*P* Value	AIC	Compare With Model
1. Fully saturated	9034.30					
2. ACE	9041.14	6.84	9	.65	–11.12	1
3. AE[b]	**9042.19**	**1.05**	**1**	**.31**	**–12.07**	**2**
4. CE	9054.19	13.06	1	.01[c]	11.06	2

Abbreviations: A, additive genetic factor; AIC, Akaike information criterion; C, shared environmental factor; E, nonshared environmental factor; –2LL, –2 log likelihood statistic; OCI-R, Obsessive-Compulsive Inventory–Revised.
[a] Boldface type indicates the best-fitting model.
[b] Standardized parameter estimates (95% confidence interval): A, 0.48 (0.37-0.52); E, 0.53 (0.47-0.59).
[c] Significant decline in fit.

DATA ANALYSES

Univariate Twin Analyses of the Broad OCD Phenotype

Univariate maximum-likelihood model-fitting analyses of raw data were conducted to partition the variance of the OCI-R total score into additive genetic (A), shared (C), and nonshared environmental (E) factors using the structural equation-modeling package Mx.[23] As is standard procedure with analysis of raw data, the data were first fitted to a saturated model,[24] and goodness of fit, in terms of a log-likelihood χ^2 statistic and Akaike information criterion, was obtained by comparing the –2 log-likelihood statistic of the more parsimonious genetic model with that of the saturated model. Because the distribution of the OCI-R was positively skewed, polychoric correlations and genetic and environmental influences on OCD were estimated using liability threshold models.[25] We used 3 thresholds, representing different categories of OC symptom severity: no symptoms (OCI-R, 0), minimal symptoms (OCI-R, 1-5), moderate symptoms (OCI-R, 6-20), and severe symptoms or "caseness" (OCI-R, ≥21). These provided a good representation of variability in symptom severity within our sample and ensured a sufficient number of cases within each category.

Multivariate Twin Analyses of OC Symptom Dimensions

Multivariate model-fitting analyses were conducted to decompose the covariances between the different OC symptom dimensions into A, C, and E factors. Three thresholds, representing the different categories of symptom severity, were specified for each of the OCI-R subscales and ranged from no symptoms (score, 0) to caseness (eg, score, ≥5 for the checking subscale; eTable 2).

To estimate MZ and DZ twin correlations within and across each of the 5 OC symptom dimensions, the data were fitted to a constrained correlational model in Mx. The MZ and DZ correlations for each of the symptom subscales (ie, the cross-twin within-subscale correlation) provided an indication of the relative contribution of genetic and environmental factors to the liability of each dimension (eg, checking). The ratio of MZ and DZ correlations across different symptom subscales (ie, the cross-twin cross-subscale correlation) provided an indication of the contribution of genetic and environmental factors to the shared liability of different symptom dimensions (eg, washing and checking).

To formally examine the genetic and environmental etiology underlying OC symptom dimensions, the data were fitted to 3 multivariate genetic models: a fully saturated triangular Cholesky decomposition, an independent pathway (IP) model, and a common pathway (CP) model.[24] The Cholesky decomposition estimates 1 A, 1 C, and 1 E factor for each of the OC symptom dimensions and makes no assumption regarding the genetic and environmental architecture underlying their comorbidity. As such, this model provides a basis against which the more parsimonious IP and CP models can be compared.

The IP model (eFigure, top) estimates 1 set of common genetic factors (A_c), shared environmental factors (C_c), and nonshared (E_c) environmental factors, which influence the covariance between OC symptoms through direct (independent) paths to each of the 5 OC symptom dimensions. In this model, specific genetic factors (A_{sp}), shared environmental factors (C_{sp}), and nonshared (E_{sp}) environmental factors are also estimated to account for the remaining symptom-specific variance. The CP model (eFigure, bottom) is nested within the IP model and provides the most parsimonious approach to the data. In this model, the covariation between the different OC symptom dimensions is influenced by a single phenotypic latent factor (ie, OCD), which combines the shared (ie, nonindependent) contribution of common A, C, and E factors. Similarly to the IP model, A, C, and E factors specific to each OC symptom dimension are estimated to account for symptom-specific variance.

To establish the best fit for the data, the Cholesky model was compared with the increasingly more parsimonious IP and CP models. Goodness of fit was established by both likelihood ratio tests and the Akaike information criterion. Alternative submodels were then tested by systematically dropping paths from the best-fitting model, and goodness of fit was established by the likelihood ratio test.

Given the large number of matrices estimated (10 × 10), implementing the maximum-likelihood raw data approach to the multivariate analyses was too computationally intensive. For this reason, polychoric correlation and asymptotic covariance matrices were computed (PRELIS 2.3[26]) for all twin pairs with complete data points (3454 participants, consisting of 917 MZ twin pairs and 810 DZ twin pairs) and analyzed in Mx by the method of asymptotic-weighted least squares.

RESULTS

UNIVARIATE TWIN ANALYSES OF THE BROAD OCD PHENOTYPE

Polychoric correlations (with 95% confidence intervals) for the OCI-R total scale were 0.47 (0.40-0.53) for MZ twins and 0.28 (0.19-0.36) for DZ twins (all $P < .001$), suggesting a model consistent with genetic variation and negligible shared environmental effects.

Results of the univariate model-fitting analyses are presented in **Table 1**. Liability thresholds could be equated across zygosity and birth order without any loss in fit ($\chi^2_9 = 6.7$; $P = .89$), indicating that the prevalence of OC symp-

©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/25/2013

Table 2. Phenotypic Correlations Between the 5 Obsessive-Compulsive Symptom Dimensions[a]

Symptom Dimension	Checking	Hoarding	Obsessing	Ordering	Washing
Checking	1.00				
Hoarding	0.48	1.00			
Obsessing	0.46	0.45	1.00		
Ordering	0.49	0.45	0.43	1.00	
Washing	0.53	0.38	0.42	0.55	1.00

[a] All correlations were significant at $P < .001$.

Table 3. Cross-Twin Within-Subscale (Diagonal) and Cross-Twin Cross-Subscale (Off-Diagonal) Correlations for MZ and DZ Female Twins[a]

Symptom Dimension	Checking	Hoarding	Obsessing	Ordering	Washing
Checking	0.38 (MZ) 0.21 (DZ)	0.22	0.29	0.26	0.28
Hoarding	0.10	0.50 (MZ) 0.27 (DZ)	0.29	0.21	0.15
Obsessing	0.09	0.13	0.49 (MZ) 0.28 (DZ)	0.26	0.21
Ordering	0.16	0.15	0.10	0.42 (MZ) 0.27 (DZ)	0.31
Washing	0.17	0.09	0.02	0.15	0.51 (MZ) 0.25 (DZ)

Abbreviations: DZ, dizygotic; MZ, monozygotic.
[a] Cross-twin cross-subscale correlations for MZ are given in the shaded area above the diagonal and for DZ twins in the clear area below the diagonal.

toms is similar for MZ and DZ twins, as well as for first- and second-born twins. Comparisons of the ACE model with the fully saturated model showed that the genetic model fit the data well. Dropping C did not result in a significant loss in fit. In contrast, dropping A resulted in a significantly worse fit to the data, indicating that additive genetic factors are important in explaining variability in this trait. Table 1 provides the standardized parameter estimates and 95% confidence intervals for the best-fitting model. Consistent with the pattern of correlations, genetic factors accounted for 48% of the variance of OC symptoms, with nonshared environmental factors and measurement error accounting for the remainder of the variance.

MULTIVARIATE ANALYSES OF OC SYMPTOM DIMENSIONS

Phenotypic correlations between the OCI-R subscales were computed across all individual twins and are given in **Table 2**. The pattern of correlations indicates significant covariation across all combinations of symptom categories. The largest correlation is seen between the ordering and washing subscales ($r = 0.55$), followed by the checking and washing subscales ($r = 0.53$). The lowest correlation is seen between the hoarding and washing subscales ($r = 0.38$).

Cross-twin within-subscale correlations for MZ and DZ twins are shown on the diagonal of **Table 3**. The pattern of correlations suggests meaningful genetic bases to the liability of each of the 5 symptom dimensions. Of note, twin correlations for the hoarding subscale (0.50 for MZ twins and 0.27 for DZ twins) are remarkably similar to those obtained with another measure of hoarding symptoms (0.52 for MZ twins and 0.27 for DZ twins) in a previous report.[27]

The cross-twin cross-subscale correlations (shown on the off-diagonal) are consistently lower for DZ twins than for MZ twins, suggesting that genetic factors are at least partly responsible for the overlap of each of the individual combinations of subscales (Table 3). The moderate MZ correlations across the different subscales ($r = 0.15$-0.31) also indicate that common nonshared environmental factors are likely to be important in explaining correlations across different symptoms.

Results of the multivariate model-fitting analyses are shown in **Table 4**. The fully saturated Cholesky decomposition model yielded a nonsignificant χ^2 value and a large and negative Akaike information criterion value, indicating a good fit to the data. The more parsimonious IP model (2) provided an excellent fit to the data, as indicated by a significant improvement in Akaike information criterion. However, the more restrictive CP model (3) produced a significantly worse fit. The IP model was therefore retained as the model of choice, and all subsequent models were compared with it.

In the next step, a series of nested submodels (4-10) were fitted to the data to test the importance of specific parameters. In these models, the genetic and environmental liabilities of each symptom dimension were either forced to be entirely independent (models 4-7) or entirely shared (models 8-10). In model 4, dropping the common genetic factor from the full IP model and forcing all genetic risk to be symptom specific produced a significantly worse fit to the data, suggesting that some of the genetic liability is shared among the different OC symptom dimensions. Similarly, forcing all environmental risk to be symp-

©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/25/2013

Table 4. Model-Fitting Results for the Cholesky, IP, and CP Models[a]

Model		Estimated Parameter: Common Factors	Estimated Parameter: Specific Factors	Fit Statistic: AWLS χ^2	Fit Statistic: *df*	Fit Statistic: *P* Value	Fit Statistic: AIC	Comparison of Nested Models: Compare With	Comparison of Nested Models: $\Delta\chi^2$	Comparison of Nested Models: Δdf	Comparison of Nested Models: *P* Value
1	Cholesky, saturated	ACE	ACE	57.39	70	.86	−82.61				
2	**IP[a]**	**ACE**	**ACE**	**70.37**	**80**	**.77**	**−89.62**	1			
3	CP	ACE	ACE	106.31	88	.09	−69.69	2	35.94	8	.001
Test of A, C, and E Factors Common to All OC Symptom Dimensions											
4	IP	CE	ACE	124.74	85	.01	−45.26	2	54.37	5	.001
5	IP	AE	ACE	99.96	85	.01	−70.04	2	29.59	5	.001
6	IP	AC	ACE	215.38	85	.01	45.38	2	145.01	5	.001
7	IP	E	ACE	309.71	90	.01	129.71	2	239.34	10	.001
Test of A, C, and E Factors Specific to Each OC Symptom Dimension											
8	IP	ACE	CE	82.12	85	.57	−87.87	2	11.75	5	.04
9	**IP[a]**	**ACE**	**AE**	**73.34**	**85**	**.76**	**−94.65**	**2**	**2.97**	**5**	**.70**
10	IP	ACE	E	186.04	90	.01	6.04	2	115.67	10	.001

Abbreviations: A, additive genetic factor; AIC, Akaike information criterion; AWLS, asymptotic-weighted least squares; C, shared environmental factor; CP, common pathway; E, nonshared environmental factor; IP, independent pathway; OC, obsessive-compulsive.
[a] Best-fitting model (in boldface type) based on AIC.

Table 5. Parameter Estimates for the Best-Fitting Independent Pathway Model[a]

Symptom	Additive Genetic Factors: Common	Additive Genetic Factors: Specific	Additive Genetic Factors: Total	Shared Environmental Factors: Common	Shared Environmental Factors: Specific	Nonshared Environmental Factors: Common	Nonshared Environmental Factors: Specific	Nonshared Environmental Factors: Total
Checking	0.27 (0.18-0.34)	0.11 (0.05-0.16)	0.38 (0.29-0.45)	0.0006[b] (0-0.06)		0.27 (0.20-0.35)	0.35 (0.27-0.43)	0.62 (0.53-0.70)
Hoarding	0.20 (0.08-0.31)	0.24 (0.15-0.30)	0.44 (0.29-0.54)	0.05 (0-0.17)		0.24 (0.17-0.31)	0.27 (0.19-0.34)	0.51 (0.43-0.58)
Obsessing	0.29 (0.15-0.47)	0.18 (0-0.26)	0.47 (0.32-0.57)	0.05 (0-0.17)		0.14 (0.08-0.19)	0.34 (0.27-0.42)	0.48 (0.39-0.56)
Ordering	0.29 (0.19-0.37)	0.15 (0.08-0.21)	0.44 (0.32-0.51)	0.0005[b] (0-0.09)		0.21 (0.15-0.27)	0.35 (0.27-0.42)	0.56 (0.47-0.64)
Washing	0.35 (0.09-0.54)	0.04[b] (0-0.21)	0.39 (0.13-0.55)	0.11 (0.003-0.33)		0.25 (0.15-0.36)	0.25 (0.10-0.35)	0.50 (0.39-0.60)

[a] Data given as parameter estimates (95% confidence intervals).
[b] Parameters can be dropped without any loss in fit.

tom specific, by dropping the shared and nonshared common environmental factors in models 5 and 6, led to a significant deterioration in fit, suggesting that some of the environmental liability is also shared. Fitting a model that assumes that all the genetic risk is shared and that there are no symptom-specific genetic influences (8) also provided a significantly worse fit to the data, suggesting that the different OC symptom dimensions are not exclusively influenced by the same genetic factors. A poor fit was also obtained by constraining all the nonshared environmental influence (and measurement error) to be the same across all OC symptom dimensions (10), suggesting that, although some of the nonshared environmental risk factors are shared, some are also unique. Dropping symptom-specific shared environmental factors from the model did not contribute to a worsening in fit (9), suggesting that these factors are not important in explaining individual differences in liability to the different OC symptom dimensions (Table 4).

The best-fitting model to the data, therefore, was model 9, in which the covariation between the 5 OC symptom dimensions is explained by a set of common A, C, and E factors, and the remainder of the variance is explained by independent A and E factors specific to each dimension. Parameter estimates for each subscale for the best-fitting model are presented in **Table 5** and **Figure 1**. Consistent with the pattern of correlations, genetic factors accounted for 38% to 44% of the variance of the individual OCI-R subscales, with nonshared environment accounting for the remainder of the variance.

Although the common shared environment factor could not be dropped from the model without deterioration in fit, this factor accounted for a negligible percentage of the overall variance (0.05%-11%) and contributed significantly only to the hoarding, obsessing, and washing subscales. That is, fixing the path from the common C factor to 0 for the checking and ordering dimensions did not worsen the fit of the model. Genetic influences that are specific to washing symptoms could also be dropped from the model without a worsening in fit, suggesting that genetic influence on this OC symptom dimension is entirely shared (asymptotic-weighted least squares $\chi^2_{88}=76.45$; $P=.80$, Akaike information criterion = −99.53, compared with model 9: $\Delta\chi^2_3=3.11$, $P=.37$; Figure 1).

Excluding the hoarding dimension from the analyses did not change the pattern of results, with the IP model still fitting the data best (data available upon request).

The extent to which genetic and environmental influence on each of the 5 symptom dimensions is shared (vs unshared) with other OC symptom dimensions can be cal-

©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/25/2013

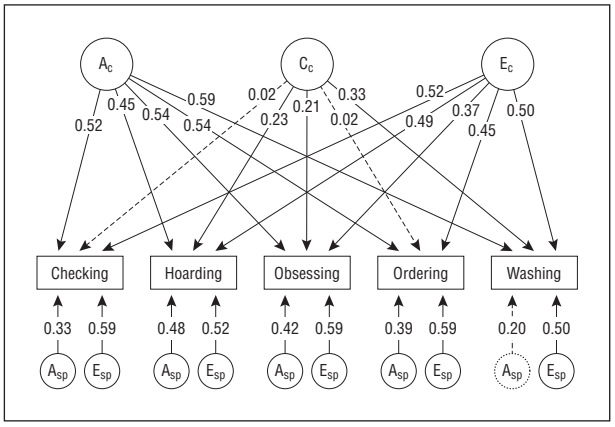

Figure 1. Path diagram for the best-fitting independent pathway model. Squaring these paths gives the proportion of variance accounted for by each common and symptom-specific factor. Dotted lines indicate that the path can be dropped from the model without any loss in fit (asymptotic-weighted least squares: χ^2_{88}=76.45, *P*=.80, Akaike information criterion=−99.53, compared with model 9: $\Delta\chi^2_3$=3.11, *P*=.37). A_c indicates common genetic factors; A_{sp}, specific genetic factors; C_c, common shared environmental factors; E_c, common nonshared environmental factors; and E_{sp}, specific nonshared environmental factors.

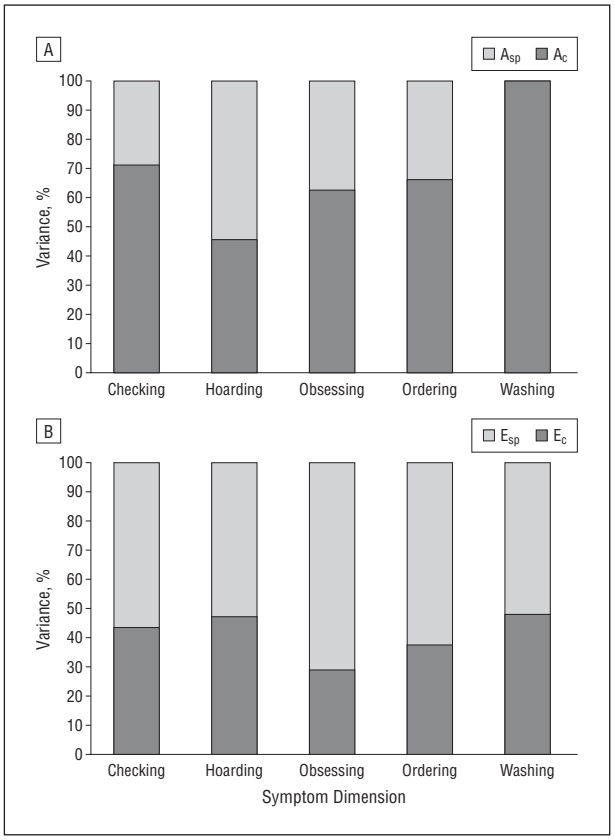

Figure 2. Percentage of the variance accounted for by common and specific genetic and nonshared environmental factors for each symptom dimension of the OCI-R based on the best-fitting model. The breakdown of the genetic and nonshared environmental variance into common and specific factors is shown in A (A_c and A_{sp}) and B (E_c and E_{sp}), respectively. OCI-R indicates Obsessive-Compulsive Inventory–Revised. See the legend to Figure 1 for definitions of the abbreviations.

culated by dividing the proportion of variance due to common effects with that due to total effects (**Figure 2**). For hoarding, up to 54.5% of the genetic variance was unshared (compared with 0%-37.5% for the other dimensions), suggesting that genetic risk factors that are independent of other OC symptom dimensions make a substantial contribution to the liability of hoarding. Nonshared environmental influence (and measurement error) was comparable across the 5 OC symptom dimensions and was mostly unshared (52.0%-71.0% due to unshared variance). For obsessing, 71.0% of the variance was unshared, suggesting that independent environmental risk factors make an important contribution to the liability of this symptom dimension.

COMMENT

A consistent body of research[1,2,4,5] indicates that OCD is a highly heterogeneous condition. A key question in our field is whether this phenotypic heterogeneity also reflects etiologic heterogeneity.[6] The present study tested one of the key assumptions of the multidimensional model of OCD, namely, that both common and specific etiologic factors are implicated in each of its major symptom dimensions.[1]

GENETIC AND ENVIRONMENTAL INFLUENCES ON THE BROAD OCD PHENOTYPE

Univariate model-fitting analyses showed that the best-fitting model for the data comprised additive genetic and nonshared environmental factors. Under this model, additive genetic factors accounted for approximately 50% of the variance of OC symptoms, with nonshared environment and measurement error accounting for the remainder. Our estimate of heritability is comparable to that obtained in other samples of adult twins (ie, 26%-55%)[28-30] and somewhat lower than that obtained in samples of child and adolescent twins (ie, 47%-61%).[31-33] In line with previous research,[28-33] environmental factors shared by siblings growing up in the same family did not influence individual variation in the liability to OCD, further suggesting that these factors may be less important in the etiology of the disorder.

GENETIC AND ENVIRONMENTAL INFLUENCES ON THE OC SYMPTOM DIMENSIONS

As expected, there was significant phenotypic overlap across the different OC symptom dimensions. We used multivariate genetic analyses to explore the extent to which this overlap was influenced by genetic and environmental factors. Specific hypotheses about the genetic and environmental structure of OC symptoms were also explored by fitting the data to a CP model and an IP model. The CP model, which assumes that the genetic and environmental causes of all OC symptom dimensions have the same underlying structure, provided a poor fit to the data. This suggests that, although the different dimensions are etiologically related to some extent, there is no underlying unitary OCD construct that can account for their covariation. Instead, we found that an IP model, which allows genetic and environmental factors to influence each dimension directly, best described our data. This was true even after the hoarding dimension was excluded from the analyses. The best-fitting model comprised additive ge-

©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/25/2013

netic and shared and nonshared environmental factors common to all OC symptom dimensions, and genetic and unique environmental factors specific to each symptom dimension. Covariation across the different dimensions was largely explained by genetic and nonshared environmental factors; although significant shared environmental effects were found, these tended to be negligible.

Additive genetic factors made a significant contribution to all the OC symptom dimensions. Heritability estimates ranged from 38% to 47% and, although broadly similar across dimension, these were somewhat greater for the obsessing (47%), hoarding (44%), and ordering (44%) subscales. These findings are consistent with those of previous research,[2,7,34-38] showing that different symptom dimensions, in particular hoarding and obsessions/checking, tend to cluster in families. They further suggest that the pattern of familiality observed in the previous studies is partly due to genetic factors.

Although we found evidence for overlap, genetic and environmental factors specific to each dimension were at least as important. The relative contribution of common vs specific genetic factors varied across dimension. In particular, we found that some dimensions were either completely (washing) or largely (ordering, checking, obsessing) influenced by common genetic factors. In contrast, hoarding had the lowest loading on the common factor and was mostly influenced by specific genetic effects (54.5% specific). If this finding were to be replicated, hoarding would share less variance with OCD than any 2 internalizing disorders do. For example, Tambs et al[39] recently estimated the degree to which genetic and environmental risk factors are shared rather than unique across 5 anxiety disorders (panic disorder, generalized anxiety disorder, phobias, OCD, and posttraumatic stress disorder). A common pathway model provided the best fit for the data, suggesting that all these disorders mostly share genetic and environmental risk factors. The amount of shared genetic variance ranged between 55% (OCD) and 96% (generalized anxiety disorder). Similar studies[40,41] have shown, for instance, that generalized anxiety disorder and depression share the same genetic risk factors. In the present study, hoarding shared only 45.5% of the genetic variance with OCD. This finding supports the notion of hoarding as an etiologically distinct, albeit related, entity from OCD and is consistent with the proposal of the new diagnostic category of hoarding disorder in *DSM-5*.[11]

Nonshared environmental factors and measurement error were also important in explaining the liability of the different OC symptom dimensions. The contribution of these factors ranged from 48% to 62% and was somewhat higher for the checking subscale. The relative contribution of common vs specific environmental factors suggested that a greater proportion of the variance was attributable to specific environmental factors to each dimension, ranging from 52% to 71%. This raises the intriguing possibility that (hoarding aside) a set of (largely) common genetic factors may predispose individuals to develop broadly defined OCD, but (largely) specific environmental risk factors may shape the specific symptomatic expression of the disorder. However, because of the cross-sectional design of this study, it was not possible to measure the extent to which nonshared environmental influences reflect the effect of instrument-common and scale-specific measurement error as opposed to "pure" nonshared environmental variance.

Our findings partially replicate those of a study[8] that used a similar methodology. The authors found evidence for a broad underlying OC phenotype influenced by genetic and nonshared environmental factors. Consistent with our data, they found that obsessing and checking were largely influenced by common genetic factors. Contrary to our data, they found that washing was largely influenced by specific genetic factors. That study was limited by the use of an instrument that lacks coverage of the full range of OC symptoms, and further research is needed to replicate our findings.

We hope that our results will encourage further research into specific biological and environmental mechanisms underlying specific OC symptom dimensions. For example, studies of MZ twins discordant for specific symptom dimensions could be used to explore dimension-specific nonshared environmental risk/protective factors.[42] Ultimately, this research may inform clinical practice, for example, via identification of dimension-specific predisposing or maintaining factors that could be targeted in treatment.

LIMITATIONS

The current study has some limitations. First, our sample was 90% female and there was insufficient power to test quantitative and qualitative sex differences in the genetic and environmental risk factors to the broad OCD phenotype and its symptom dimensions. Second, because OC symptoms were measured at a single time point, it was not possible to estimate measurement error and adjust heritability and nonshared environment estimates accordingly. Studies clarifying the extent to which "pure" nonshared environmental factors contribute to these traits are needed. Third, OC symptoms were measured by self-report and were not validated by clinical interview. However, the OCI-R subscales are valid measures of OCD symptom subtypes in both clinical and nonclinical populations and correlate highly with clinician-administered measures.[16,18] Fourth, a maximum likelihood estimation of raw data would have been preferable to the asymptotic least-squares estimation used in this study because this approach facilitates inclusion of twins with missing data and affords greater statistical power and precision. Finally, our findings should be interpreted in view of the more general limitations of the twin design.[25] Triangulating twin studies, such as the present one, with family and adoption studies would be a helpful strategy to address this issue.

In conclusion, obsessive compulsive disorder is unlikely to be etiologically homogeneous. Symptom dimension–specific genetic, and particularly nonshared environmental, factors are at least as important as shared etiologic factors. We recommend including the major symptom dimensions of OCD as specifiers in *DSM-5*, along with detailed descriptions in the accompanying text. Hoarding shares less than 50% of genetic variance with the remaining symptom dimensions, which is consistent with the emerging view that hoarding may be an etiologically distinct subtype or even a separate disorder from OCD.

©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/25/2013

Submitted for Publication: September 14, 2010; final revision received December 7, 2010; accepted December 28, 2010.
Correspondence: David Mataix-Cols, PhD, Departments of Psychosis Studies and Psychology, King's College London, Institute of Psychiatry, PO 69, De Crespigny Park Rd, London SE5 8AF, England (david.mataix-cols@kcl.ac.uk).
Financial Disclosure: None reported.
Funding/Support: The Department of Twin Research is supported by the Wellcome Trust and the Department of Health via the National Institute for Health Research–comprehensive Biomedical Research Centre award to Guy's & St Thomas' National Health Service Foundation Trust in partnership with King's College London.
Online-Only Material: The eTables and eFigure are available at http://www.archgenpsychiatry.com.

REFERENCES

1. Mataix-Cols D, Rosario-Campos MC, Leckman JF. A multidimensional model of obsessive-compulsive disorder. *Am J Psychiatry*. 2005;162(2):228-238.
2. Leckman JF, Rauch SL, Mataix-Cols D. Symptom dimensions in obsessive-compulsive disorder. *CNS Spectr*. 2007;12(5):376-387, 400.
3. Bloch MH, Landeros-Weisenberger A, Rosario MC, Pittenger C, Leckman JF. Meta-analysis of the symptom structure of obsessive-compulsive disorder. *Am J Psychiatry*. 2008;165(12):1532-1542.
4. Baer L. Factor analysis of symptom subtypes of obsessive compulsive disorder and their relation to personality and tic disorders. *J Clin Psychiatry*. 1994;55 (suppl):18-23.
5. Leckman JF, Denys D, Simpson HB, Mataix-Cols D, Hollander E, Saxena S, Miguel EC, Rauch SL, Goodman WK, Phillips KA, Stein DJ. Obsessive-compulsive disorder. *Depress Anxiety*. 2010;27(6):507-527.
6. Taylor S. Dimensional and subtype models of OCD. In: Abramowitz JS, Houts AC, eds. *Concepts and Controversies in Obsessive-Compulsive Disorder*. New York, NY: Springer; 2005:27-41.
7. Katerberg H, Delucchi KL, Stewart SE, Lochner C, Denys DA, Stack DE, Andresen JM, Grant JE, Kim SW, Williams KA, den Boer JA, van Balkom AJ, Smit JH, van Oppen P, Polman A, Jenike MA, Stein DJ, Mathews CA, Cath DC. Symptom dimensions in OCD. *Behav Genet*. 2010;40(4):505-517.
8. van Grootheest DS, Boomsma DI, Hettema JM, Kendler KS. Heritability of obsessive-compulsive symptom dimensions. *Am J Med Genet B Neuropsychiatr Genet*. 2008; 147(4):473-478.
9. Moore J, Smith GW, Shevlin M, O'Neill FA. Alternative factor models and heritability of the Short Leyton Obsessional Inventory–Children's Version. *J Abnorm Child Psychol*. 2010;38(7):921-934.
10. van Grootheest DS, Cath DC, Beekman AT, Boomsma DI. Twin studies on obsessive-compulsive disorder: a review. *Twin Res Hum Genet*. 2005;8(5):450-458.
11. Mataix-Cols D, Frost RO, Pertusa A, Clark LA, Saxena S, Leckman JF, Stein DJ, Matsunaga H, Wilhelm S. Hoarding disorder: a new diagnosis for *DSM-V*? *Depress Anxiety*. 2010;27(6):556-572.
12. Pertusa A, Frost RO, Fullana MA, Samuels J, Steketee G, Tolin D, Saxena S, Leckman JF, Mataix-Cols D. Refining the diagnostic boundaries of compulsive hoarding: a critical review. *Clin Psychol Rev*. 2010;30(4):371-386.
13. Spector TD, Williams FM. The UK Adult Twin Registry (TwinsUK). *Twin Res Hum Genet*. 2006;9(6):899-906.
14. Andrew T, Hart DJ, Snieder H, de Lange M, Spector TD, MacGregor AJ. Are twins and singletons comparable? *Twin Res*. 2001;4(6):464-477.
15. Sarna S, Kaprio J, Sistonen P, Koskenvuo M. Diagnosis of twin zygosity by mailed questionnaire. *Hum Hered*. 1978;28(4):241-254.
16. Foa EB, Huppert JD, Leiberg S, Langner R, Kichic R, Hajcak G, Salkovskis PM. The Obsessive-Compulsive Inventory. *Psychol Assess*. 2002;14(4):485-496.
17. Noble M, McLennan D, Wilkinson K, Whitworth A, Barnes H, Dibben C. *The English Indices of Deprivation 2007*. London, England: Communities and Local Government; 2008. http://www.communities.gov.uk/documents/communities/pdf/733520.pdf. Accessed November 2010.
18. Abramowitz JS, Deacon BJ. Psychometric properties and construct validity of the Obsessive-Compulsive Inventory–Revised: replication and extension with a clinical sample. *J Anxiety Disord*. 2006;20(8):1016-1035.
19. Rosario-Campos MC, Miguel EC, Quatrano S, Chacon P, Ferrao Y, Findley D, Katsovich L, Scahill L, King RA, Woody SR, Tolin D, Hollander E, Kano Y, Leckman JF. The Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS). *Mol Psychiatry*. 2006;11(5):495-504.
20. Pertusa A, Jaurrieta N, Real E, Alonso P, Bueno B, Segalàs C, Jiménez-Murcia S, Mataix-Cols D, Menchón JM. Spanish adaptation of the Dimensional Yale-Brown Obsessive-Compulsive Scale. *Compr Psychiatry*. 2010;51(6):641-648.
21. Pertusa A, Fernández de la Cruz L, Alonso P, Menchón JM, Mataix-Cols D. Independent validation of the Dimensional Yale-Brown Obsessive Compulsive Scale (DY-BOCS). *Eur Psychiatry*. In press.
22. Gönner S, Hahn S, Leonhart R, Ecker W, Limbacher K. Identification of main symptoms in OCD patients by use of symptom scales. [in German] *Verhaltenstherapie*. 2009;19:251-258. doi:10.1159/000236897.
23. *Mx: Statistical Modelling*. 6th ed, version 1.54a. Richmond, VA: Dept of Psychiatry, VCU; 2002. http://www.vcu.edu/mx/. Accessed November 2010.
24. Neale MC, Cardon LR. *Methodology for Genetic Studies of Twins and Families*. Dordrecht, the Netherlands: Kluwer Academic Publishers; 1992.
25. Rijsdijk FV, Sham PC. Analytic approaches to twin data using structural equation models. *Brief Bioinform*. 2002;3(2):119-133.
26. PRELIS 2.3 [computer program]. Chicago, IL: Scientific Software International Inc; 1999.
27. Iervolino AC, Perroud N, Fullana MA, Guipponi M, Cherkas L, Collier DA, Mataix-Cols D. Prevalence and heritability of compulsive hoarding: a twin study. *Am J Psychiatry*. 2009;166(10):1156-1161.
28. Clifford CA, Murray RM, Fulker DW. Genetic and environmental influences on obsessional traits and symptoms. *Psychol Med*. 1984;14(4):791-800.
29. Jonnal AH, Gardner CO, Prescott CA, Kendler KS. Obsessive and compulsive symptoms in a general population sample of female twins. *Am J Med Genet*. 2000; 96(6):791-796.
30. Van Grootheest DS, Cath DC, Beekman AT, Boomsma DI. Genetic and environmental influences on obsessive-compulsive symptoms in adults: a population-based twin-family study. *Psychol Med*. 2007;37(11):1635-1644.
31. Hudziak JJ, Van Beijsterveldt CE, Althoff RR, Stanger C, Rettew DC, Nelson EC, Todd RD, Bartels M, Boomsma DI. Genetic and environmental contributions to the Child Behavior Checklist Obsessive-Compulsive Scale: a cross-cultural twin study. *Arch Gen Psychiatry*. 2004;61(6):608-616.
32. van Grootheest DS, Bartels M, Cath DC, Beekman AT, Hudziak JJ, Boomsma DI. Genetic and environmental contributions underlying stability in childhood obsessive-compulsive behavior. *Biol Psychiatry*. 2007;61(3):308-315.
33. Bolton D, Rijsdijk F, O'Connor TG, Perrin S, Eley TC. Obsessive-compulsive disorder, tics and anxiety in 6-year-old twins. *Psychol Med*. 2007;37(1):39-48.
34. Alsobrook JP II, Leckman JF, Goodman WK, Rasmussen SA, Pauls DL. Segregation analysis of obsessive-compulsive disorder using symptom-based factor scores. *Am J Med Genet*. 1999;88(6):669-675.
35. Hasler G, Pinto A, Greenberg BD, Samuels J, Fyer AJ, Pauls D, Knowles JA, McCracken JT, Piacentini J, Riddle MA, Rauch SL, Rasmussen SA, Willour VL, Grados MA, Cullen B, Bienvenu OJ, Shugart Y-Y, Liang K-Y, Hoehn-Saric R, Wang Y, Ronquillo J, Nestadt G, Murphy DL; OCD Collaborative Genetics Study. Familiality of factor analysis-derived YBOCS dimensions in OCD-affected sibling pairs from the OCD Collaborative Genetics Study. *Biol Psychiatry*. 2007;61(5):617-625.
36. Pinto A, Greenberg BD, Grados MA, Bienvenu OJ III, Samuels JF, Murphy DL, Hasler G, Stout RL, Rauch SL, Shugart YY, Pauls DL, Knowles JA, Fyer AJ, McCracken JT, Piacentini J, Wang Y, Willour VL, Cullen B, Liang K-Y, Hoehn-Saric R, Riddle MA, Rasmussen SA, Nestadt G, Farkas KJ. Further development of YBOCS dimensions in the OCD Collaborative Genetics study. *Psychiatry Res*. 2008;160(1):83-93.
37. Cullen B, Brown CH, Riddle MA, Grados MA, Bienvenu OJ, Hoehn-Saric R, Shugart YY, Liang K-Y, Samuels J, Nestadt G. Factor analysis of the Yale-Brown Obsessive Compulsive Scale in a family study of obsessive-compulsive disorder. *Depress Anxiety*. 2007;24(2):130-138.
38. Chacon P, Rosario-Campos MC, Pauls DL, Hounie AG, Curi M, Akkerman F, Shimabokuro FH, de Mathis MA, Lopes AC, Hasler G, Miguel EC. Obsessive-compulsive symptoms in sibling pairs concordant for obsessive-compulsive disorder. *Am J Med Genet B Neuropsychiatr Genet*. 2007;144B(4):551-555.
39. Tambs K, Czajkowsky N, Røysamb E, Neale MC, Reichborn-Kjennerud T, Aggen SH, Harris JR, Ørstavik RE, Kendler KS. Structure of genetic and environmental risk factors for dimensional representations of *DSM-IV* anxiety disorders. *Br J Psychiatry*. 2009;195(4):301-307.
40. Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. Major depression and generalized anxiety disorder. *Arch Gen Psychiatry*. 1992;49(9):716-722.
41. Roy MA, Neale MC, Pedersen NL, Mathé AA, Kendler KS. A twin study of generalized anxiety disorder and major depression. *Psychol Med*. 1995;25(5):1037-1049.
42. Cath DC, van Grootheest DS, Willemsen G, van Oppen P, Boomsma DI. Environmental factors in obsessive-compulsive behavior: evidence from discordant and concordant monozygotic twins. *Behav Genet*. 2008;38(2):108-120.

©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/25/2013