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Etiology of obsessions and compulsions: A meta-analysis and narrative review of twin studies

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ABSTRACT

The relative importance of genetic and environmental factors in the etiology of obsessive–compulsive (OC) symptoms is unclear. Cognitive–behavioral models propose that shared environment (e.g., parenting style) is important. Family segregation studies suggest that nonadditive genetic factors may be involved. To investigate the etiology of OC symptoms, a meta-analysis was conducted of 37 twin samples from 14 studies, supplemented by a narrative review. Results indicated that in terms of mean effect sizes, (a) additive genetic effects and nonshared environment accounted for most of the variance in OC symptoms, (b) shared environment and nonadditive genetic effects made little or no contribution; (c) these findings did not vary with sex or symptom severity; (d) variance due to nonshared environment increased with age; (e) gene-environment interactions play an etiologic role; (f) OC symptoms are shaped by etiologic factors common to all types of OC symptoms but also have symptom-specific etiologies; and (g) OC symptoms are also shaped by very general etiologic factors (e.g., those influencing negative emotionality). Overall, the findings indicate that OC symptoms have a complex etiologic architecture that is not adequately explained by contemporary etiological models.

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1. Introduction

Obsessive–compulsive disorder (OCD) is characterized by obsessions and compulsions. Obsessions are unwanted and distressing thoughts, images, or urges. Compulsions are repetitive behaviors or mental acts that the person feels compelled to perform, typically with a desire to resist. OCD has an estimated lifetime prevalence of 2 to 3% in the general population (Kessler, Berglund, Demler, Jin, & Walters, 2005) and is associated with considerable suffering, functional impairment, and economic burden to both the individual and the health-care system (Knapp, Henderson, & Patel, 2000).

Much remains to be learned about the etiology of obsessive–compulsive (OC) symptoms. Studies of monozygotic (MZ) and dizygotic (DZ) twin pairs have been conducted to investigate several kinds of etiologic factors, including additive genetic effects (A), nonadditive genetic effects (D), shared environment (C), and nonshared environment (E). Additive genetic effects are those in which the probability of occurrence, or severity, of a given phenotype (e.g., a symptom or disorder) is influenced by many genes, which additively combine in their effects. Nonadditive genetic effects include epistatic effects (gene-gene interactions) and dominance effects. Shared environment includes experiences shared by both members of a twin pair, such as the experience of being raised by parents who exhibit particular parenting styles, such as a tendency to be critical and overcontrolling. Nonshared environment includes experiences that are not shared by members of a twin pair, such as a stressful life event experienced by one twin but not his or her co-twin. In twin studies, nonshared environment also includes error variance, which can be minimized by using psychometrically sound measures and by using structural equation modeling methods that explicitly model error variance (e.g., see Taylor, Jang, & Asmundson, 2010b).

Twin studies are important for several reasons. First, they can shed light on the etiologic architecture of psychopathologic phenomena, including information about the relative importance of genetic and environmental factors, and information about whether two or more clinical phenomena (e.g., checking compulsions and hoarding behaviors) are etiologically related to one another. Second, twin studies can yield useful information for guiding molecular genetic research, such as information about whether a given phenotype (e.g., the diagnostic category of OCD or the total score on a global measure of OC symptoms) is etiologically homogeneous or heterogeneous. Replication failure in molecular genetic research is a common problem, and such studies are more likely to be fruitful when they focus on etiologically homogeneous phenomena (Haworth & Plomin, 2010; Wood & Neale, 2010). Third, consistent the current zeitgeist concerning translational research, findings from basic research (e.g., twin studies) may eventually be translated into practical applications, such as matching etiologic profiles to specific treatments.

Most twin studies of OC phenomena have been based on community samples in which OC symptoms were measured dimensionally, rather than using the diagnosis of OCD as the unit of analysis. This is because OC symptoms in nonclinical samples are in many ways similar to the symptoms of people meeting diagnostic criteria for OCD (Taylor et al., 2010b). These studies, as reviewed in detail later in this article, generally show that A and E each account for a significant proportion of variance in OC symptoms. The roles of C and D are less clear. Studies of other (non-OC) forms of psychopathology suggest that C may have small-to-moderate effect sizes (10 to 30% of variance; Burt, 2009). D effects might have a similar magnitude. Twin studies typically have not had sufficient statistical power to detect effects of this size (Kendler & Prescott, 2006).

Are C and D likely to play a role in OC symptoms? Contemporary cognitive–behavioral models (e.g., Clark, 2004; Frost & Steketee, 2002; Salkovskis, Shafran, Rachman, & Freeston, 1999) propose that particular early learning experiences (e.g., parental criticism and overcontrol) give rise to particular types of dysfunctional beliefs (e.g., perfectionistic beliefs and beliefs that one is highly responsible for preventing harm befalling oneself and others). These beliefs are said to give rise to OC symptoms. Accordingly, cognitive–behavioral models suggest that C plays an important role in OC symptoms.

Results from family segregation studies suggest that D might also be involved in shaping OC symptoms. Segregation analysis is a form of statistical modeling of the pattern of inheritance among probands diagnosed with OCD and their biological relatives. Segregation analysis uses Maximum Likelihood (ML) estimation to compare the goodness-of-fit of various inheritance models to the observed data. This method can be used to test whether the pattern of inheritance of OC symptoms or OCD is most consistent with A, D, or some combination of the two (Abel & Dessein, 1998). Segregation studies have provided suggestive evidence of D effects, although these studies have so far failed to unambiguously demonstrate that a model consisting D effects has a better goodness-of-fit than a model consisting of A effects or a model consisting of both A and D (Pauls, 2010).

An aim of the present study was to determine, by means of a meta-analysis of twin data, whether C and D contribute significant variance to OC symptoms. Meta-analysis involves the pooling of data across studies and often has greater statistical power than individual studies (Borenstein, Hedges, Higgins, & Rothstein, 2009b). There have been no previously published meta-analyses of OC symptoms or OCD, as indicated by literature searches of MEDLINE, PubMed, PsychINFO, and EMBASE. Each database was searched because they are not entirely overlapping in content (Lefebvre, Manheimer, & Glanville, 2008). For studies included in the meta-analysis, within-pair MZ and DZ correlations were extracted and biometric structural equation modeling was used to decompose the correlations into variance components due to A, C, or E (ACE model), or into components due to A, D, and E (ADE model). C and D cannot be simultaneously estimated on the basis of within-pair MZ and DZ correlations (Neale & Maes, 2004).[1]

Each variance component (A, C, and E for the ACE model, and A, D, and E for the ADE model) was treated as an effect size and separately meta-analyzed. Analyses were also conducted to determine whether there was significant variability (heterogeneity) in effect sizes across samples; that is, variability in excess of that due to random error. If such variability was detected, then subgroup analyses were conducted to determine whether heterogeneity was due to categorical methodological factors (e.g., type of assessment instrument). Meta-regression was also conducted to determine whether heterogeneity of effect size could be attributed to continuous variables such as age at assessment. The meta-analysis was conducted and reported in accordance with the guidelines of the American Psychological Association Publications and Communications Board Working Group on Journal Article Reporting Standards (2008).

For findings from twin studies that were not amenable to meta-analysis, such as when there were too few studies of a given research issue (i.e., fewer than 5 studies per research question; Borenstein et al., 2009b), a narrative review conducted. This addressed issues concerning (a) etiological differences and similarities between different types of OC symptoms, (b) whether these symptoms are shaped by etiologic factors that are very general in their influence (e.g., those shaping neuroticism or negative emotionality), (c) whether findings from community samples can be generalized to subsamples with clinically elevated symptoms, and (d) whether OC symptoms are influenced by gene-environment interactions.

[1] Twin studies use structural equation modeling to estimate unknown parameters (A, C, D, and E) from estimates of known parameters (e.g., within-pair correlations of MZ and DZ twin pairs). To solve the simultaneous equations used in structural equation modeling, it is necessary that there is a greater number of known than unknown parameters. Accordingly, it is possible to separately test ACE and ADE models, but C and D cannot be estimated simultaneously.

In summary, a combination of meta-analysis and narrative review was conducted in order to synthesize and describe the current state of knowledge concerning the etiologic architecture of OC phenomena, as revealed by twin studies.

2. Method

2.1. Literature search and study selection criteria

For both the meta-analysis and narrative review, studies were included if the following criteria were met: (a) The study was designed to yield OC data on A, C, and E (or A, D, E), using pairs of MZ and DZ twins. These were typically studies that explicitly reported such analyses, although articles only reporting within-pair correlations were potentially eligible for inclusion. (b) The study used a validated measure of OC symptoms or a structured diagnostic measure of OCD. Studies using symptom measures were included in the meta-analysis only if they used a measure assessing a range of OC symptoms (global OC symptom severity) rather than only assessing a single type of symptom. Relevant studies were identified by systematically searching MEDLINE, PubMed, PsychINFO, and EMBASE. Databases were searched for articles published up to September, 2011. Search terms were *obsess**, *compuls**, *gene**, and *twin**. The asterisks denote the use of wild cards; for example, *obsess** includes terms such as *obsession*, *obsessions*, and *obsessive*. References cited in the identified articles, and references cited in related review articles and book chapters, were also examined. The search not limited to English-language articles, although no relevant articles in other languages were identified.

Fourteen eligible studies yielding 37 samples were included in the meta-analysis (Table 1). All were studies of twins recruited from the community and used either OC symptom severity assessments or diagnostic assessments of OCD. Table 1 shows that the number of MZ pairs in each sample was similar to, or more often larger, than the number of DZ pairs. This pattern was reversed for Bolton, Rijsdijk, O'Connor, Perrin, and Eley (2007). Accordingly, the lead author of that study was contacted in order to check whether the sample sizes were correct. The samples sizes were verified as accurate (Derek Bolton, Ph.D., personal communication, February, 2011).

A number of studies were excluded from the meta-analysis. The rationales are as follows. Two studies (Hur, 2009; Taylor, Asmundson, & Jang, 2011) were excluded from the meta-analyses because they were secondary analyses of other studies (Hur & Jeong, 2008; Taylor et al., 2010b). Iervolino et al. (2009) was excluded from the meta-analysis because only compulsive hoarding was assessed. For studies omitted from the meta-analysis, salient findings are covered in the narrative review.

Three twin studies were identified that did not report results for ACE or ADE models but might have yielded data (e.g., within

Table 1
Characteristics of samples included in the meta-analysis.

Sample	MZ pairs: *N*	DZ pairs: *N*	r_{MZ}	r_{DZ}	Mean age in years (and SD)	Sex	Language of assessment	Measure
Clifford et al. (1984)	250	198	.458	.144	31 (12)	33%♂	English	LOI
Jonnal, Gardner, Prescott, and Kendler (2000)	334	193	.310	.100	36 (8)	♀	English	PI-20
Eley et al. (2003): Female	818	760	.580	.280	4 (<1)	♀	English	CBC-M
Eley et al. (2003): Male	723	769	.590	.190	4 (<1)	♂	English	CBC-M
Hudziak et al. (2004): Female 7 yo	822	634	.570	.210	7 (<1)	♀	Dutch	CBC
Hudziak et al. (2004): Male 7 yo	760	651	.550	.310	7 (<1)	♂	Dutch	CBC
Hudziak et al. (2004): Female 9 yo	242	204	.460	.100	9 (2)	♀	English	CBC
Hudziak et al. (2004): Male 9 yo	300	280	.510	.340	9 (1)	♂	English	CBC
Hudziak et al. (2004): Female 10 yo	593	429	.540	.220	10 (<1)	♀	Dutch	CBC
Hudziak et al. (2004): Male 10 yo	506	443	.590	.350	10 (<1)	♂	Dutch	CBC
Hudziak et al. (2004): Female 12 yo	330	240	.500	.400	12 (<1)	♀	Dutch	CBC
Hudziak et al. (2004): Male 12 yo	277	233	.570	.300	12 (<1)	♂	Dutch	CBC
Bolton et al. (2007)	253	601	.570	.220	6 (<1)	49%♂	English	ADIS
van Grootheest et al. (2008): Female 12 yo	162	124	.450	.360	12 (<1)	♀	Dutch	CBC-A
van Grootheest et al. (2008): Male 12 yo	140	138	.500	.380	12 (<1)	♂	Dutch	CBC-A
van Grootheest et al. (2008): Female 14 yo	222	144	.600	.300	14 (<1)	♀	Dutch	CBC-A
van Grootheest et al. (2008): Male 14 yo	134	128	.570	.170	14 (<1)	♂	Dutch	CBC-A
van Grootheest et al. (2008): Female 16 yo	209	189	.580	.330	16 (<1)	♀	Dutch	CBC-A
van Grootheest et al. (2008): Male 16 yo	175	130	.450	.300	16 (<1)	♂	Dutch	CBC-A
Hur and Jeong (2008): Female	337	65	.390	.360	17 (2)	♀	Korean	MOCI
Hur and Jeong (2008): Male	186	60	.560	.240	17 (2)	♂	Korean	MOCI
Tambs et al. (2009): Female	446	264	.350	.320	28 (NR)	♀	Norwegian	CIDI
Tambs et al. (2009): Male	219	117	.450	.200	28 (NR)	♂	Norwegian	CIDI
van Grootheest et al. (2009): Female, M = 18 yo	380	280	.350	.250	18 (2)	♀	Dutch	CBC-M
van Grootheest et al. (2009): Male, M = 18 yo	273	231	.410	.100	18 (2)	♂	Dutch	CBC-M
van Grootheest et al. (2009): Female, M = 20 yo	422	258	.530	.250	20 (3)	♀	Dutch	CBC-M
van Grootheest et al. (2009): Male, M = 20 yo	272	223	.390	.240	20 (3)	♂	Dutch	CBC-M
van Grootheest et al. (2009): Female, M = 26 yo	407	244	.470	.320	26 (10)	♀	Dutch	CBC-M
van Grootheest et al. (2009): Male, M = 25 yo	216	147	.460	.110	25 (10)	♂	Dutch	CBC-M
van Grootheest et al. (2009): Female, M = 33 yo	631	293	.440	.210	33 (12)	♀	Dutch	PI-12
van Grootheest et al. (2009): Male, M = 33 yo	236	99	.370	.350	33 (12)	♂	Dutch	PI-12
Taylor et al. (2010b)	167	140	.507	.315	40 (15)	22%♂	English	OCI-R
Moore, Smith, Shevlin, and O'Neill (2010): Female	54	36	.300	.406	12 (1)	♀	English	LOI-CV
Moore et al. (2010): Male	39	43	.678	.361	12 (1)	♂	English	LOI-CV
Fagnani et al. (2011)	159	180	.470	.170	23–24 yo	45%♂	Italian	SCL-90
Iervolino et al. (2011)	971	857	.470	.280	56 (13)	♀	English	OCI-R
Lahey et al. (2011)	1571 pairs[a]		.640	.320	9–17 yo	Mixed[b]	English	CAPS

ADIS = Anxiety Disorders Interview Schedule; CAPS = Child and Adolescent Psychopathology Scale; CBC = Obsessive–Compulsive Scale from the Child Behavior Checklist; CBC-A = Adolescent version of the Obsessive–Compulsive Scale from the Child Behavior Checklist; CBC-M = modified OC scale based on items from the Child Behavior Checklist; CIDI = Composite International Diagnostic Inventory; DZ = izygotic; LOI = Leyton Obsessional Inventory; LOI-CV = short form of the children's version of the Leyton Obsessional Inventory; MOCI = Maudsley Obsessional–Compulsive Inventory; MZ = Monozygotic; NR = not reported (age range 19–36 years); OCI-R = Obsessive Compulsive Inventory-Revised; PI-12, and PI-20 = respectively, the 12 and 20 item versions of the Padua Inventory; SCL-90 = OC scale from the 90-item Symptom Checklist-Revised.

[a] Only the combined number of MZ and DZ pairs was reported.

[b] Proportions of males and females were not reported.

twin-pair correlations) relevant for the evaluation of such models (Andrews, Stewart, Allen, & Henderson, 1990; Skre, Torgersen, Lygren, & Kringlen, 1993; Young, Fenton, & Lader, 1971). None of these studies were included for the following reasons. Andrews et al. (1990) was omitted because within-pair correlations were not reported and could not be computed from the information reported in that study. Young et al. (1971) was omitted because the sample was too small to yield reliable estimates of within-pair correlations ($N = 17$ MZ and 15 DZ pairs), as indicated by the implausible value of $r_{DZ} = -.380$. DZ twins share 50% of their segregating genes, and so even if the heritability of OC symptoms was zero, r_{DZ} should not be less than zero. The study by Skre et al. (1993, $N = 20$ MZ pairs and 29 DZ pairs), which reported twin data on the diagnosis of OCD, was omitted for similar reasons. Although these authors did not report within-pair correlations, intra-class within-pair correlations were computed by the present author based on MZ and DZ concordance data described by Skre et al. These values were $r_{MZ} = .782$ and $r_{DZ} = -.018$. The values are most probably unreliable due to the small N and low base-rate of OCD in the sample. Although the differences between these MZ and DZ correlations might appear dramatically different, they are based on minor differences in concordances. For MZ twins, 5/40 individuals were diagnosed with OCD; two pairs were concordant and one pair was discordant for the disorder. For DZ twins, 2/58 individuals were diagnosed with OCD in which no pairs were concordant and two pairs were discordant for OCD. Given these small samples and minor differences in concordances, the within-pair intra-class MZ and DZ correlations are likely to be unreliable and are, in fact, anomalous when compared to the within-pair correlations in Table 1.

Some samples included in the meta-analysis were overlapping; that is, samples of people assessed over time, coming from two longitudinal research programs. One was the Netherlands Twin Registry, consisting of samples from van Grootheest et al. (2008) and van Grootheest, Cath, Hottenga, Beekman, and Boomsma, (2009) and all samples from Hudziak et al. (2004) except for their 9-year-old male and female samples, which came from a different (U.S.) twin registry. The other set of overlapping samples was from a British longitudinal study (Bolton et al., 2007; Eley et al., 2003). Overlapping samples were included in the meta-analysis to maximize statistical power. Effects of sample overlap were investigated by re-running the meta-analysis in which the effect sizes within each set of overlapping samples were averaged. That is, the two sets of overlapping samples yielded three sets of mean results (Dutch males, Dutch females, and British males and females), which when added to the other, nonoverlapping samples, yielded a total of 17 samples. Note that the Hudziak 9-year-old samples were included as separate samples in these analyses. Note also that for the averaged analysis of the British samples, it was not possible to split the sample into separate groups of males and females.

2.2. Assessment measures

Almost all of the OC measures in Table 1 were dimensional measures of overall, current OC symptom severity. There were three exceptions. Lahey, Van Hulle, Singh, Waldman, and Rathouz (2011) assessed symptom severity over the past 12 months. Bolton et al. (2007) and Tambs et al. (2009) administered diagnostic measures of lifetime prevalence. Bolton et al. classified cases on a 2-point scale; 0 = no OCD, 1 = subclinical OCD or full OCD as defined by DSM-IV (American Psychiatric Association, 2000). Subclinical OCD was diagnosed when a person met all DSM-IV criteria for OCD except the impairment criterion. Tambs et al. used a 3-point scale; 0 = no OCD, 1 = subclinical, and 2 = full OCD as defined by DSM-IV.

Each assessment measure in Table 1 has at least some degree of psychometric data supporting its reliability and validity as a research instrument. But none are perfect instruments and some have been criticized in the literature. For example, the OC scale from the Symptom Checklist-90 has been criticized because it measures a mix of OC symptoms and general distress (Taylor, 1995). The OC scale from the Child Behavior Checklist was criticized in terms of its psychometric properties by Storch et al. (2006), although other studies have found that the scale performed well on various indices of reliability and validity (Geller et al., 2006; Hudziak et al., 2006; Nelson et al., 2001). In the meta-analysis reported below, subgroup analyses were conducted to determine whether a given OC scale yielded anomalous results and whether effect sizes were related to the reliability of the symptom scales (as estimated by Cronbach's α).[2]

2.3. Statistical methods

2.3.1. Alpha level

Given the large number of analyses reported in this article, an α level of .01 was used, along with corresponding 99th percentile confidence intervals, instead of the conventional α level of .05. This was done in order to reduce Type I error without unduly inflating Type II error.

2.3.2. Computation of genetic and environmental variance components

Within-pair MZ and DZ correlations form the basis of computing the values of the ACE and ADE models. Twin studies are based on the degree of similarity within pairs of twins for a given variable. MZ twins share 100% of their segregating genes whereas DZ twins share approximately 50%. Heritability estimates for a given variable are based on the within-pair similarity of MZ pairs compared to that of DZ pairs. In general, larger MZ than DZ within-pair correlations for a given variable indicate the presence of genetic effects because the greater MZ similarity is attributed to the twofold greater genetic similarity of MZ than DZ twins. All within-pair correlations in Table 1 were derived from the original articles, except for Tambs et al. (2009), for which the values were obtained by contacting the lead investigator. All correlations in Table 1 were Pearson's r, with the following exceptions: Three studies (Iervolino, Rijsdijk, Cherkas, Fullana, & Mataix-Cols, 2011; Tambs et al., 2009; van Grootheest et al., 2008) used polychoric r, Bolton et al. (2007) reported tetrachoric r, and Hur and Jeong (2008) computed ML-based r. Sensitivity analyses (described below) were used to gauge whether a given study yielded anomalous results because of using, for example, a correlation coefficient other than Pearson's r.

Using the *Mx* statistical program (Neale, Boker, Xie, & Maes, 2006), MZ and DZ within-pair correlations for each sample were decomposed by means of structural equation modeling into variance components due to A, C, and E, or due to A, D, and E. For each variance component of each sample, the 99th percentile confidence interval was computed. These intervals were based on ML estimation rather than on the computation of standard errors, because the latter produce values that are out of bounds (i.e., less than 0 or greater than 1) and are constrained to be symmetric, whereas confidence intervals of variance components are often empirically found to be asymmetric (Neale & Miller, 1997).

2.3.3. Meta-analytic methods

Meta-analyses – including tests of effect size heterogeneity and moderator analyses (subgroup analyses and meta-regressions) – were conducted using the *Comprehensive Meta-Analysis* (*CMA*) software, version 2.205 (Borenstein, Hedges, Higgins, & Rothstein,

[2] Coefficient α is only an approximate index of scale reliability, and was included in the present study because it was the only reliability coefficient that was available for most of the symptom rating scales.

2009a). Random effects modeling was used because it was unclear whether the true effect size for a given variable was the same across all studies. That is, the true effect sizes might differ as a function of age, sex, or other variables.

For the computation of main effects of A, D, C, and E, analyses were conducted across all samples and then repeated after controlling for overlapping samples. This was done by computing the weighted (random effects) mean effect sizes within each of the Netherlands and British samples and then entering those means into the pool of effect sizes used in the meta-analysis.

In consultation with two experts on meta-analysis (Michael Borenstein, Ph.D., and Larry V. Hedges, Ph.D., personal communications, August, 2010), the following procedure was used to meta-analyze the variance components in a way that is consistent with the use of ML-based confidence intervals. This involved a version of the inverse variance method (Borenstein et al., 2009b) in which more precise studies (i.e., those with smaller ML confidence intervals and typically larger sample sizes) received greater weighting. For each sample, each variance component (A, D, C, and E) was treated as an effect size akin to Cohen's *d*. The effect size for each sample was inversely weighted by an ML-derived value that was akin to the standard error; that is, weighting = 1/((width of ML-based confidence interval)/(2*2.576)). The value 2.576 is the *Z* score corresponding to the 99th percentile confidence interval.

CMA was used to compute the weighted means of A, D, C, and E. *Mx* was then used to compute the ML-based 99th percentile confidence intervals around each of the means. This was done by way of path tracing rules. To illustrate, for the ACE model, *CMA* provided mean values of A and C that were used to compute the mean within-pair correlations; $r_{MZ} = A + C$ and $r_{DZ} = 0.5 * A + C$. The correlations were used to calculate, via *Mx*, the ML-based confidence intervals around the mean values of A, C, and E. A similar procedure was used for the ADE model, where $r_{MZ} = A + D$ and $r_{DZ} = 0.5 * A + 0.25 * D$. The confidence intervals were used to test whether the weighted mean values of A, D, C, and E were significantly different from zero.

To determine if the results for a given variance component were unduly influenced by the results from any one sample, sensitivity analysis were conducted by re-computing the mean effect size after omitting each sample, one at a time. This made it possible to determine whether the pattern of results significantly changed when any one study was omitted from the meta-analysis.

Publication bias – the selective publication of significant results – is an issue of relevance for many types of meta-analysis, particularly for those concerning treatment outcome studies. However, it is unclear whether this form of bias would play much of a role in twin studies, because all outcomes are newsworthy, such as findings that OC symptoms are entirely due to A and E, entirely due to E, and so-forth. Nevertheless, publication bias was examined by calculating Rosenthal's (1979) fail-safe *N*, which is the number of unpublished, nonsignificant studies required to lead an observed mean effect size to become nonsignificant at the specified α level of .01. The larger the fail-safe *N*, the less likely it is that unpublished, nonsignificant studies would alter the observed pattern of results.

For each variance component, heterogeneity of effect sizes was tested with the *Q* statistic, which has a χ^2 distribution. If significant heterogeneity was detected, then mixed effects subgroup analyses were conducted to determine if effect sizes varied as a function of the following variables: Language of assessment (scored as 1 = English, 2 = Dutch, 3 = other), method of assessment (1 = symptom rating scale, 2 = structured diagnostic interview), type of symptom rating scale (1 = Leyton Obsessional Inventory for either children or adults, 2 = Padua Inventory, 3 = Child Behavior Checklist OC scale, as adapted for either children/adolescents or adults, 4 = Maudsley Obsessional–Compulsive Inventory, 5 = Obsessive–Compulsive Inventory, revised, 6 = other), and sex (coded as 1 = all male sample, 2 = all female sample; mixed samples were excluded from analyses of sex differences).

To further explore to possible reasons for effect size heterogeneity, random effect meta-regressions (using the method of moments) were conducted, with each sample weighted according to the inverse variance method. *CMA* permits only a single predictor to be entered in each meta-regression, and so more than one meta-regression was conducted for each variance component. Predictor variables were Cronbach's α and age at the time of assessment. The majority of samples were quite homogeneous in terms of age (see Table 1), which made these samples suitable for meta-regression.

2.3.4. Statistical power

The statistical power of the present study to detect significant C and D effects was calculated by means of a script from the *Mx* library (http://www.psy.vu.nl/mxbib/index.php?page=mx_tree&tree_list=1,49,50,54&last=54 downloaded December, 2009).

3. Meta-analytic results

Based on the sample sizes in Table 1, and using 99th percentile ML-based confidence intervals and for mean values of A ranging from .300 to .600, there was sufficient (>.80) statistical power to detect C values as small as .067 (i.e., 6.7% of phenotypic variance) and D values as small as .133 (13.3%). Therefore, the present study had sufficient statistical power to detect small C and D effects.

Tables 2 and 3 show the weighted mean effect sizes for the variance components of the ACE and ADE models. Note that A + C + E and A + D + E should both sum to 1.000. This was not quite the case in the tables because of rounding error. Nevertheless, mean results based all 37 samples (second last row of each table) were consistent with mean results in which the effect sizes of the overlapping samples were averaged (the last row of each table). Both tables show that the mean A and E effects were statistically significant, with A accounting for 37 to 41% of variance, and E accounting for 50 to 52% of variance. These estimates varied only slightly across models (ACE vs. ADE) and samples (all samples vs. nonoverlapping samples). Table 2 shows that C effects were marginally significant only for the overall set of samples, but substantively C accounted for only a small proportion of variance (5 to 6%). None of the individual studies in Table 2 obtained significant C effects; all confidence intervals overlapped with zero. It was only with the large pooled sample used in the meta-analysis that it was possible to detect marginally statistically significant but small C effects. Table 3 shows that D effects were nonsignificant, accounting for 9 to 10% of variance. D effects may have become significant with greater statistical power. But even if a larger sample had been available, it appears that D effects would have been small, at best accounting for only a small fraction of phenotypic variance.

Sensitivity analyses for the overall sample indicated that the pattern of results did not change with the removal of any given sample from the meta-analysis, for any given variance component. That is, there was no evidence that the results were distorted by outliers. Fail-safe *N* was computed for A and C for analyses based on all samples (i.e., the most powerful condition). This analysis was not computed for D effects, which were nonsignificant and so Fail-safe *N* was not relevant. Fail-safe *N* for E was not computed because E is always significant because it includes residual error.

Over 3000 studies obtaining nonsignificant A effects, and over 190 studies obtaining nonsignificant C effects, would have been required to render the observed mean effect sizes nonsignificant. This suggests that publication bias was unlikely to have influenced the pattern of weighted means obtained in the present meta-analysis.

According to the *Q* statistic, there was significant across-sample heterogeneity of effect sizes for each of A, C, E (ACE model) and for A, D, E (AD model), for both the overall and nonoverlapping samples. That is, heterogeneity attributable to variation in true effect sizes (i.e., in excess of that attributable to random error). For all 37 samples for

Table 2
ACE model: meta-analysis of additive genetic factors (A), shared environment (C), and nonshared environment (E): proportions of explained variance (and their 99th percentile confidence intervals).

Sample	A	C	E
Clifford et al. (1984)	.440 (.163–.554)	.000 (.000–.221)	.560 (.446–.692)
Jonnal et al. (2000)	.299 (.000–.414)	.000 (.000–.273)	.702 (.586–.828)
Eley et al. (2003): Female	.578 (.406–.630)	.000 (.000–.149)	.422 (.370–.480)
Eley et al. (2003): Male	.570 (.485–.627)	.000 (.000–.062)	.430 (.373–.494)
Hudziak et al. (2004): Female 7 yo	.559 (.450–.614)	.000 (.000–.090)	.441 (.386–.502)
Hudziak et al. (2004): Male 7 yo	.480 (.275–.607)	.070 (.000–.247)	.450 (.393–.515)
Hudziak et al. (2004): Female 9 yo	.430 (.200–.548)	.000 (.000–.178)	.570 (.452–.707)
Hudziak et al. (2004): Male 9 yo	.340 (.019–.598)	.170 (.000–.431)	.490 (.396–.605)
Hudziak et al. (2004): Female 10 yo	.533 (.358–.599)	.000 (.000–.149)	.468 (.401–.542)
Hudziak et al. (2004): Male 10 yo	.480 (.245–.651)	.110 (.000–.312)	.410 (.346–.486)
Hudziak et al. (2004): Female 12 yo	.200 (.000–.537)	.300 (.000–.522)	.500 (.407–.611)
Hudziak et al. (2004): Male 12 yo	.540 (.204–.658)	.030 (.000–.318)	.430 (.342–.539)
Bolton et al. (2007)	.543 (.365–.633)	.000 (.000–.120)	.458 (.367–.563)
van Grootheest et al. (2008): Female 12 yo	.180 (.000–.576)	.270 (.000–.522)	.550 (.412–.713)
van Grootheest et al. (2008): Male 12 yo	.240 (.000–.622)	.260 (.000–.541)	.500 (.366–.672)
van Grootheest et al. (2008): Female 14 yo	.600 (.204–.691)	.000 (.000–.350)	.400 (.309–.518)
van Grootheest et al. (2008): Male 14 yo	.549 (.234–.677)	.000 (.000–.245)	.451 (.323–.617)
van Grootheest et al. (2008): Female 16 yo	.500 (.131–.677)	.080 (.000–.389)	.420 (.323–.545)
van Grootheest et al. (2008): Male 16 yo	.300 (.000–.582)	.150 (.000–.480)	.550 (.417–.716)
Hur and Jeong (2008): Female	.060 (.000–.490)	.330 (.000–.489)	.610 (.500–.729)
Hur and Jeong (2008): Male	.558 (.059–.670)	.000 (.000–.454)	.442 (.331–.582)
Tambs et al. (2009): Female	.060 (.000–.409)	.290 (.000–.420)	.650 (.551–.748)
Tambs et al. (2009): Male	.446 (.004–.567)	.000 (.000–.380)	.554 (.433–.698)
van Grootheest et al. (2009): Female, M = 18 yo	.200 (.000–.454)	.150 (.000–.381)	.650 (.544–.769)
van Grootheest et al. (2009): Male, M = 18 yo	.383 (.138–.500)	.000 (.000–.188)	.617 (.500–.748)
van Grootheest et al. (2009): Female, M = 20 yo	.528 (.238–.607)	.000 (.000–.255)	.472 (.393–.564)
van Grootheest et al. (2009): Male, M = 20 yo	.300 (.000–.508)	.090 (.000–.389)	.610 (.492–.749)
van Grootheest et al. (2009): Female, M = 26 yo	.300 (.000–.553)	.170 (.000–.445)	.530 (.441–.633)
van Grootheest et al. (2009): Male, M = 25 yo	.438 (.150–.562)	.000 (.000–.231)	.562 (.438–.708)
van Grootheest et al. (2009): Female, M = 33 yo	.439 (.150–.513)	.000 (.000–.256)	.561 (.487–.645)
van Grootheest et al. (2009): Male, M = 33 yo	.040 (.000–.484)	.330 (.000–.480)	.630 (.500–.764)
Taylor et al. (2010b)	.384 (.000–.630)	.123 (.000–.481)	.493 (.369–.652)
Moore et al. (2010): Female	.000 (.000–.555)	.342 (.000–.560)	.658 (.426–.920)
Moore et al. (2010): Male	.634 (.000–.827)	.044 (.000–.610)	.322 (.173–.608)
Fagnani et al. (2011)	.451 (.099–.586)	.000 (.000–.267)	.549 (.415–.711)
Iervolino et al. (2011)	.380 (.187–.526)	.090 (.000–.252)	.530 (.472–.595)
Lahey et al. (2011)	.640 (.457–.684)	.000 (.000–.166)	.360 (.316–.411)
Weighted means			
All samples	**.405 (.349–.460)**	**.052 (.005–.101)**	**.509 (.492–.526)**
Nonoverlapping samples	**.384 (.302–.462)**	.058 (.000–.128)	**.522 (.497–.548)**

Statistically significant weighted means are highlighted in bold.

A, C, E and for A, D, E, $\chi^2(df = 36) > 201.98$, $p < .001$, and I^2 (proportion of observed variance due to true differences in effect size, beyond that attributable to random error) > 59%. For nonoverlapping samples, $\chi^2(df = 16) > 131.89$, $p < .001$, and $I^2 > 56\%$. Thus, there was significant heterogeneity, with for both the overall and nonoverlapping samples. Details of these and other supplementary analyses appear in the Appendix.

Subgroup analyses and meta-regressions were conducted in an effort to identify the sources of heterogeneity in effect sizes. The initial set of analyses concerned methodological factors, including type of symptom rating scale, its reliability (as gauged by Cronbach's α), language of assessment, and whether the assessment was a symptom severity rating or diagnostic assessment. None of these variables predicted the effect sizes of either A, C, D, or E ($ps > .02$; see Appendix for details).

Table 4 shows the results of the age and sex. Here, analyses were conducted for the all samples and repeated for samples consisting only of those from the Netherlands Twin Registry, which is a longitudinal study in which twins were repeatedly evaluated. There were several consistent findings. Biological sex was consistently unrelated to the magnitude of either A, D, C, or E. Age was unrelated to A, C, and D effects, but was significantly related to E (Table 4). E significantly increased as a function of age at assessment, as illustrated in Fig. 1, which shows the regression line for relationship between E and age for the ACE model. Circle diameters correspond to the relative weights assigned to the studies, according to the inverse variance method.

Given that the proportion of variance explained by E increased with age, and the total explained variance is fixed (i.e., A + C + E = A + D + E = 1.000 or 100%), then the importance of the other variance components (A, C, and D) must have decreased with age. None of these components were significant in the meta-regressions when tested individually (Table 4), which suggests that the combined effects (A + C and A + D) must have decreased with age. The interaction between age and sex in the prediction of the variance components was not investigated due to insufficient sample size. This remains a topic for future investigation. A further question for future research is whether the importance of genetic and environmental factors varies as a function of age of onset of OC symptoms. People with early onset OCD, compared to their late onset counterparts, have a greater prevalence of OCD among their first degree relatives (Taylor, 2011). Accordingly, it may be that the importance of genetic and environmental influences on OC symptoms varies as a function of the age of onset of OC symptoms or OCD.

In summary, the meta-analytic results indicated that (a) A and E, but not C and D, accounted for a significant amount of variance in OC symptoms (in terms of mean effect sizes). (b) There was significant heterogeneity of effect sizes, suggesting that the effects of A, C, D, and E might significantly vary with methodological variables and/or variables defining subpopulations. (c) Heterogeneity in effect size for E could be at least partly accounted for in terms of age. (d) None

Table 3
ADE model: meta-analysis of additive genetic factors (A), nonadditive genetic factors (D), and nonshared environment (E): proportions of explained variance (and their 99th percentile confidence intervals).

Sample	A	D	E
Clifford et al. (1984)	.118 (.000–.542)	.340 (.000–.570)	.542 (.430–.677)
Jonnal et al. (2000)	.090 (.000–.410)	.220 (.000–.428)	.690 (.572–.822)
Eley et al. (2003): Female	.540 (.188–.629)	.040 (.000–.401)	.420 (.368–.479)
Eley et al. (2003): Male	.170 (.000–.517)	.420 (.062–.640)	.410 (.356–.472)
Hudziak et al. (2004): Female 7 yo	.270 (.000–.594)	.300 (.000–.613)	.430 (.377–.491)
Hudziak et al. (2004): Male 7 yo	.556 (.290–.611)	.000 (.000–.271)	.444 (.389–.505)
Hudziak et al. (2004): Female 9 yo	.000 (.000–.516)	.458 (.000–.571)	.542 (.429–.678)
Hudziak et al. (2004): Male 9 yo	.527 (.181–.614)	.000 (.000–.352)	.473 (.387–.575)
Hudziak et al. (2004): Female 10 yo	.340 (.000–.593)	.200 (.000–.592)	.460 (.394–.536)
Hudziak et al. (2004): Male 10 yo	.598 (.312–.659)	.000 (.000–.289)	.402 (.342–.472)
Hudziak et al. (2004): Female 12 yo	.523 (.245–.607)	.000 (.000–.278)	.477 (.393–.574)
Hudziak et al. (2004): Male 12 yo	.572 (.000–.658)	.000 (.000–.600)	.428 (.342–.531)
Bolton et al. (2007)	.310 (.000–.616)	.260 (.000–.640)	.430 (.343–.542)
van Grootheest et al. (2008): Female 12 yo	.476 (.000–.601)	.000 (.000–.520)	.525 (.399–.677)
van Grootheest et al. (2008): Male 12 yo	.527 (.041–.647)	.000 (.000–.494)	.473 (.353–.625)
van Grootheest et al. (2008): Female 14 yo	.600 (.000–.691)	.000 (.000–.668)	.400 (.308–.514)
van Grootheest et al. (2008): Male 14 yo	.110 (.000–.660)	.460 (.000–.690)	.430 (.310–.594)
van Grootheest et al. (2008): Female 16 yo	.586 (.012–.680)	.000 (.000–.586)	.414 (.321–.530)
van Grootheest et al. (2008): Male 16 yo	.464 (.000–.589)	.000 (.000–.548)	.536 (.411–.686)
Hur and Jeong (2008): Female	.400 (.000–.507)	.000 (.000–.480)	.600 (.493–.720)
Hur and Jeong (2008): Male	.400 (.000–.669)	.160 (.000–.667)	.440 (.329–.581)
Tambs et al. (2009): Female	.377 (.093–.468)	.000 (.000–.286)	.623 (.532–.722)
Tambs et al. (2009): Male	.350 (.000–.566)	.100 (.000–.567)	.550 (.428–.695)
van Grootheest et al. (2009): Female, M = 18 yo	.368 (.000–.466)	.000 (.000–.400)	.633 (.534–.741)
van Grootheest et al. (2009): Male, M = 18 yo	.000 (.000–.478)	.410 (.000–.523)	.590 (.477–.726)
van Grootheest et al. (2009): Female, M = 20 yo	.470 (.000–.606)	.060 (.000–.588)	.470 (.391–.562)
van Grootheest et al. (2009): Male, M = 20 yo	.401 (.000–.512)	.000 (.000–.477)	.599 (.489–.725)
van Grootheest et al. (2009): Female, M = 26 yo	.483 (.096–.566)	.000 (.000–.393)	.518 (.434–.613)
van Grootheest et al. (2009): Male, M = 25 yo	.000 (.000–.542)	.460 (.000–.579)	.540 (.421–.687)
van Grootheest et al. (2009): Female, M = 33 yo	.400 (.000–.513)	.040 (.000–.501)	.560 (.484–.643)
van Grootheest et al. (2009): Male, M = 33 yo	.392 (.000–.514)	.000 (.000–.466)	.608 (.486–.749)
Taylor et al. (2010b)	.518 (.000–.635)	.000 (.000–.587)	.482 (.365–.626)
Moore et al. (2010): Female	.355 (.000–.590)	.000 (.000–.554)	.645 (.410–.949)
Moore et al. (2010): Male	.680 (.000–.827)	.000 (.000–.812)	.320 (.173–.580)
Fagnani et al. (2011)	.210 (.000–.579)	.260 (.000–.601)	.530 (.398–.700)
Iervolino et al. (2011)	.480 (.273–.534)	.000 (.000–.212)	.520 (.466–.580)
Lahey et al. (2011)	.640 (.282–.684)	.000 (.000–.364)	.360 (.316–.409)
Weighted means			
All samples	**.386 (.290–.479)**	.097 (.000–.195)	**.495 (.479–.511)**
Nonoverlapping samples	**.370 (.228–.474)**	.091 (.000–.237)	**.508 (.484–.533)**

Statistically significant weighted means are highlighted in bold.

of the variables available for inclusion in the meta-analysis were able to account for the heterogeneity in A, C, or D effects. This is an issue for further investigation. (e) Effect sizes obtained from studies using diagnostic measures of OCD (Bolton et al., 2007; Tambs et al., 2009) were not significantly different from those based on OC symptom measures.

Table 4
Predicting A, C, D, and E from sample sex and age.

Samples	Predictors	ACE model			ADE model		
		A	C	E	A	D	E
All samples							
	Significance: $\chi^2(df=1)$						
	Sex	1.07	0.19	1.25*	0.04	0.90**	1.54
	Age	4.64	0.98	13.10***	0.41	1.50	14.47***
	Explained variance (%)						
	Sex	0	0	0	0	0	2
	Age	28	7	37	0	0	38
Samples from the Netherlands Twin Registry							
	Significance: $\chi^2(df=1)$						
	Sex	0.30	0.14	0.24	1.04	0.79	0.11
	Age	4.54	0.27	13.68***	1.43	0.00	15.61***
	Explained variance (%)						
	Sex	2	0	0	0	0	0
	Age	31	0	56	9	0	62

Sex was coded 1 = male, 2 = female. A = additive genetic effects, C = shared environment, D = nonadditive genetic effects, and E = nonshared environment.
* $p<.01$.
** $p<.005$.
*** $p<.001$.

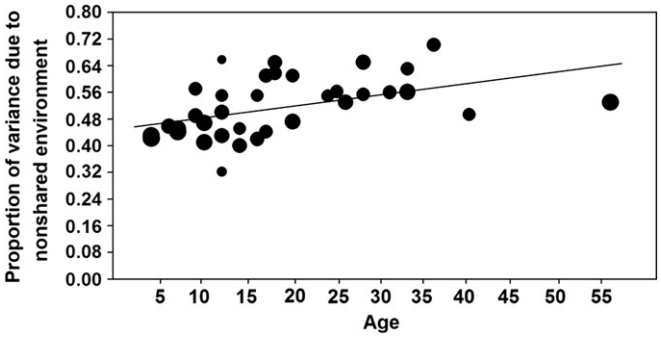

Fig. 1. Meta-regression predicting nonshared environment (E) from age at assessment, based on ACE model. Circle diameters are proportional to the weights assigned the samples.

4. Narrative review of other salient findings

4.1. Generalization of findings across levels of symptom severity

The meta-analysis suggested that effect sizes from OC symptom rating scales were no different from effect sizes from OCD diagnostic ratings, with A and E being most important. Results of a participant stratification analysis by Taylor et al. (2010b) were consistent with this finding. The magnitude of A and E effects did not differ when results for the overall community-based twin sample were compared with results from participants with relatively high scores on measures of OC symptoms (i.e., OC symptom severity scores above the 50th percentile of the sample). However, further research is needed to determine whether very severe OCD is influenced by the same sets of genetic and environmental factors that play a role in mild OC symptoms.

4.2. OC symptom subtypes

Two twin studies conducted a comprehensive evaluation of the importance of genetic and environmental factors for each of the major, empirically defined, subtypes of OC symptoms (Iervolino et al., 2011; Taylor et al., 2010b). The results, based on the same measure of symptoms (the revised Obsessive–Compulsive Inventory; Foa et al., 2002), were remarkably consistent across studies. Fig. 2 summarizes the results in terms of weighted mean effect sizes.[3]

The results show that washing, and to a lesser extent other OC symptoms, were strongly shaped by etiologic factors common to all other OC symptoms. Hoarding symptoms were among those that had the least etiologic resemblance with other OC symptoms. This is consistent with the current DSM-V proposal to define a new clinical category, hoarding disorder, which is said to fall with the spectrum of OC related disorders (Pertusa et al., 2010). Hoarding disorder is thought to be etiologically related to, but distinct from, other OC-related phenomena. This conjecture is supported by the etiologic results summarized in Fig. 2. That is, hoarding symptoms do have genetic and environmental variance in common with other OC symptoms, but hoarding tended to have a greater proportion of symptom-specific genetic and environmental variance.

4.3. Gene–environment interactions

Taylor et al. (2010b) found evidence of gene–environment interactions; that is, A-by-E interactions significantly predicted variance in OC symptoms above and beyond variance due to A and E main effects. Thus, the effects of A and E identified in the meta-analysis can be partitioned into main effects and an interaction. Such results were obtained for each of the OC symptom subtypes described in Fig. 2.

4.4. Etiological relationship with other symptoms, traits, or disorders

Table 5 shows the proportions of genetic and nonshared environmental variance of OC symptoms or disorder shared with other non-OC symptoms, traits, or disorders. Cohen's (1988) classification scheme was used to facilitate the interpretation of findings, where large effects are defined by $r \geq .50$ (i.e., ≥25% shared variance) and medium (moderate) effect sizes are defined by $r \geq .30$ (≥9% shared variance). Large and medium effects are flagged in the table. The table shows that OC symptoms had a medium or large amount of shared genetic variance with many different forms of psychopathology, but comparatively less overlapping environmental variance. The genetic findings are consistent with studies of other forms of psychopathology in which general (pleiotropic) genetic factors have been identified, playing a role in many different kinds of psychopathology (Haworth & Plomin, 2010).

Table 5 shows that OC symptoms and negative emotionality had a large amount of shared genetic variance, with a weighted mean of 37% overlapping variance across three studies (Clifford, Murray, & Fulker, 1984; Hur, 2009; Taylor et al., 2010b). In comparison, OC symptoms and negative emotionality had only a moderate amount of overlapping variance due to environmental effects; weighted mean = 12% overlapping variance. Taylor et al. (2010b) found that OC symptoms and negative emotionality were influenced by a common genetic factor but arose from different environmental factors. OC symptoms also were shaped by symptom-specific genetic factors. Similar findings were reported by Lahey et al. (2011).

Table 5 shows that OC symptoms and OC personality traits had a large amount of shared genetic variance but only had a moderate amount of overlapping environmental variance. Taylor et al. (2011) found that OC symptoms and OC personality traits had a common genetic influence, but differed in their environmental influences.

Table 5 further indicates that OC symptoms had a large amount of overlapping genetic variance with symptoms of social anxiety or interpersonal discomfort (i.e., shyness/inhibition, interpersonal sensitivity), and with symptoms of agoraphobia, separation anxiety, and major depressive disorder. OC symptoms or disorder had a moderate amount of overlapping genetic variance with many other measures of anxiety-related psychopathology, with tic disorders, and with features of attention deficit hyperactivity disorder (i.e., inattentiveness, hyperactivity/impulsivity). The amount of overlapping environmental variance with these variables was largely trivial, being mostly less than 2% (Table 5).

In terms of the relationship between OC symptom and psychotic features, the findings of Fagnani et al. (2011) merit particular consideration because the proportion of shared variance in this study tended to be much higher than the proportions reported in most of the other studies in Table 5. Those authors, using data from a community sample, claimed that three of their scales (interpersonal sensitivity, paranoid ideation, and psychoticism) all measured psychotic features, and concluded that OC symptoms and psychotic features have common genetic and environmental etiologies. There are several problems with this conclusion. Fagnani et al. used the Symptom Checklist-90, revised (SCL-90; Derogatis, 1975), which is problematic for the purpose of examining the genetic and environmental variance shared between OC symptoms and psychotic symptoms. The SCL-90 scales contain many items that measure general (nonspecific) distress, and so correlations among it scales may be spuriously inflated because they all measure, to some extent, a common variable (general distress) (Taylor, 1995). Fagnani et al. used the SCL-90 interpersonal sensitivity scale as a measure of psychotic

[3] Only weighted means were computed, rather than a full meta-analysis, because there were only two relevant studies that were available. Note also that in the Fig. 2, only Taylor, Jang et al. assessed neutralizing symptoms.

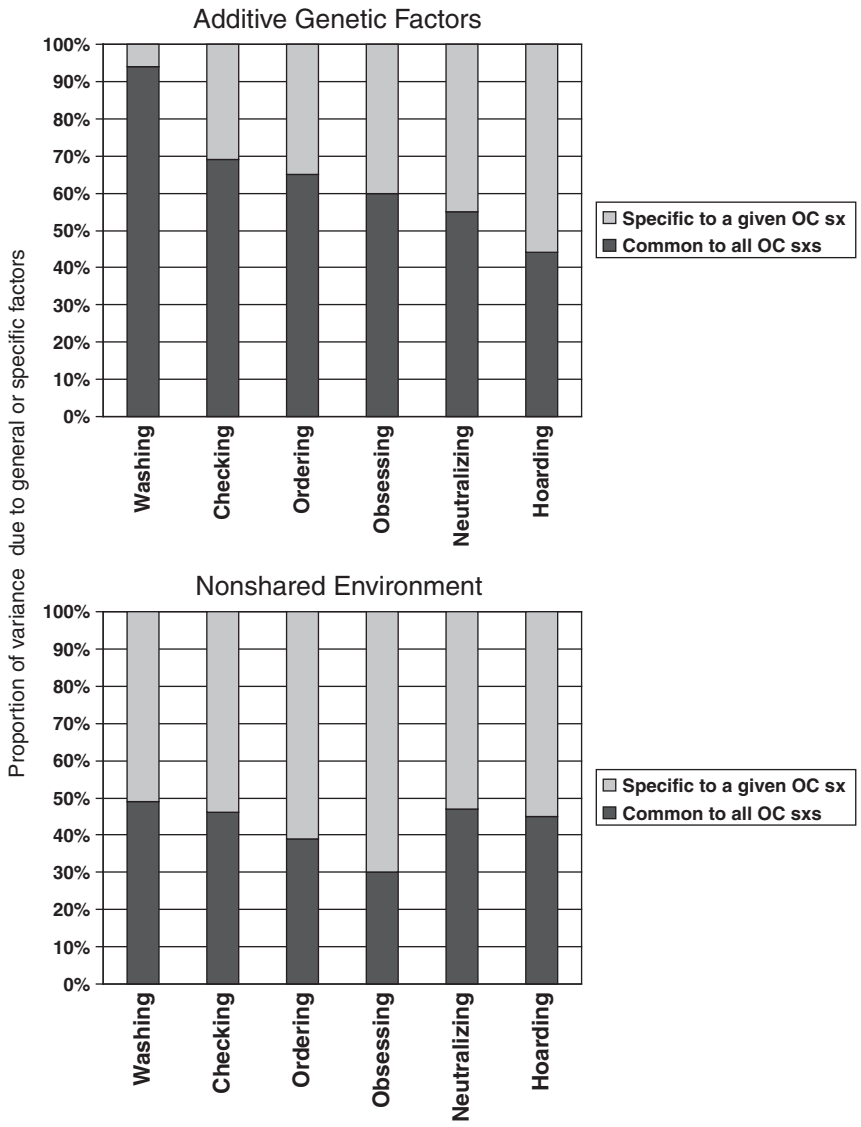

Fig. 2. Proportions of variance in OC symptom scores due to general (across all OC symptoms) or symptom-specific etiologic factors. The upper panel shows the relative importance of general and specific additive genetic factors and the lower panel shows the relative importance of general and specific nonshared environmental factors. Results were based on the weighted values (weighted by sample size) from Taylor et al. (2010b) and Iervolino et al. (2011).

features. Inspection of the item content reveals that the scale measures interpersonal discomfort, including fear of negative evaluation. Interpersonal discomfort is a nonspecific feature of many different forms of psychopathology (e.g., anxiety disorders, major depressive disorder, personality disorders, psychotic disorders) and so it cannot be claimed that it specifically measures psychotic symptoms. A further problem concerns the 10 item SCL-90 scale that purportedly measured psychoticism. Half of the items are nonspecific in that they could refer to psychotic symptoms or to features of OCD. For example, the item "Having thoughts about sex that bother you" could refer to sexual obsessions; "The idea that you should be punished for your sins" could refer to scrupulosity obsessions; and "The idea that something serious is wrong with your body" could refer to somatic obsessions. The item "The idea that something is wrong with your mind" could reflect a person's appraisals of the meaning of obsessional thoughts (see Frost & Steketee, 2002). Even the six item SCL-90 paranoid ideation scale contains items referring to awareness that other people do not share one's ideas (which might be construed as insight into one's obsessions), and that people are negatively judging the person (which may occur if a person with OCD is criticized for engaging in compulsive rituals). Accordingly, the very high proportions of overlapping variance between OC symptoms and so-called psychotic symptoms (Table 5) may have been an artifact, due to criterion contamination (i.e., the scales measured overlapping symptom domains). Further research, using methodologically rigorous methods, is needed to determine whether OC symptoms are etiologically related to psychotic symptoms.

4.5. Toward a biopsychosocial model of OC symptoms

Taylor and Jang (2011) recently evaluated the role of genetic and environmental factors in a broader, biopsychosocial context, in a way that integrates behavioral-genetics with contemporary cognitive–behavioral models. The latter propose that OC symptoms arise from particular kinds of dysfunctional beliefs, where the strength of belief influences the development and severity of OC symptoms (Clark, 2004; Frost & Steketee, 2002; Salkovskis et al., 1999). Three intercorrelated sets of beliefs have been theoretically and empirically linked to OC symptoms: (a) Perfectionism and intolerance of uncertainty (PC), (b) overimportance of thoughts and the need to control thoughts (ICT), and (c) inflated responsibility and the overestimation

Table 5
Proportions of genetic and environmental variance of OC symptoms or disorder shared with other symptoms, traits, or disorders.

OC variable	Comparison variable	Nature of comparison variable	Study	% overlapping A	% overlapping E
S	Negative emotionality	T	Clifford et al. (1984)	36**	4
S	Negative emotionality	T	Hur (2009)	26**	15*
S	Negative emotionality	T	Taylor et al. (2010b)	65**	17*
S	Traits of OC personality disorder	T	Taylor et al. (2011)	32**	13*
S	Symptoms of general distress	S	Eley et al. (2003)	7	2
S	Separation anxiety	S	Eley et al. (2003)	1	1
S	Phobic anxiety	S	Eley et al. (2003)	3	2
S	Shyness/inhibition	S	Eley et al. (2003)	35**	7
S	Major depressive disorder	S	Lahey et al. (2011)	25**	2
S	Generalized anxiety disorder	S	Lahey et al. (2011)	23*	2
S	Social anxiety disorder	S	Lahey et al. (2011)	10*	2
S	Specific phobia	S	Lahey et al. (2011)	22*	1
S	Agoraphobia	S	Lahey et al. (2011)	29**	<1
S	Separation anxiety disorder	S	Lahey et al. (2011)	46**	3
S	Conduct disorder	S	Lahey et al. (2011)	4	1
S	Inattentiveness	S	Lahey et al. (2011)	9*	1
S	Hyperactivity/impulsivity	S	Lahey et al. (2011)	19*	<1
S	Oppositional-defiant disorder	S	Lahey et al. (2011)	8	1
S	Interpersonal sensitivity	S/T	Fagnani et al. (2011)	98**	19*
S	Paranoid ideation	S/T	Fagnani et al. (2011)	79**	13*
S	Psychoticism (schizoptypal features)	S/T	Fagnani et al. (2011)	69**	26**
D	Any anxiety disorder other than OCD	Dx	Bolton et al. (2007)	7	<1
D	Any tic disorder	Dx	Bolton et al. (2007)	9*	2

A = additive genetic factors; Dx = lifetime diagnosis; E = nonshared environment; S = current symptoms; S/T = Fagnani et al. (2011) regarded these as symptoms although they could be equally regarded as personality traits; T = trait variable.
* Medium effects (≥9% overlapping variance).
** Large effects (≥25% overlapping variance).

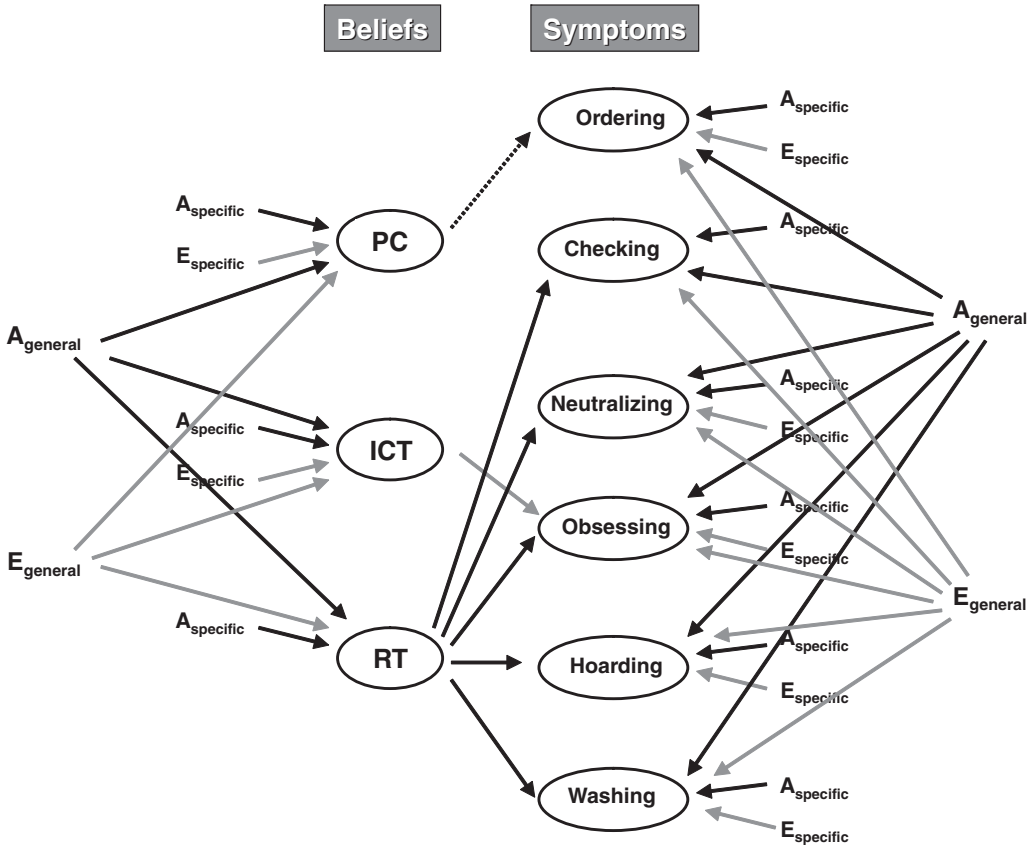

Fig. 3. An empirically derived biopsychosocial model of OC symptoms, based on twin research, in which additive genetic effects, nonshared environment, and dysfunctional beliefs influence OC symptoms. Here, belief specific and general genetic factors ($A_{specific}$, $A_{general}$) and belief specific and general environmental factors ($E_{specific}$, $E_{general}$) influence dysfunctional beliefs, which in turn influence obsessive–compulsive symptoms. The latter symptoms are also directly influenced by their own set of OC specific and general genetic factors ($A_{specific}$, $A_{general}$) and environmental factors ($E_{specific}$, $E_{general}$). ICT = overimportance and need to control thoughts; PC = perfectionism and intolerance of uncertainty; RT = inflated responsibility and overestimation of threat; Symptoms = major OC symptoms. Each arrow represents a statistically significant pathway ($p < .001$, based on a Bonferroni correction). *Source*: Taylor and Jang (2011). Biopsychosocial etiology of obsessions and compulsions: An integrated behavioral-genetic and cognitive-behavioral analysis. *Journal of Abnormal Psychology*, 120, 174–186. Reprinted by permission of the American Psychological Association.

of threat (RT) (Obsessive Compulsive Cognitions Working Group, 2005; Taylor et al., 2010a). PC involves beliefs that mistakes and imperfection are intolerable, along with beliefs that it is necessary and possible to be completely certain that aversive events will not occur. ICT entails beliefs that the mere presence of unwanted thoughts indicates that such thoughts are important or portentous (e.g., the belief that "Bad thoughts, even unwanted ones, lead to bad deeds"), along with beliefs that complete control over one's thoughts is necessary and possible. RT includes beliefs that aversive events are quite likely to occur and that one has a duty to prevent such events.

Although there is evidence supporting contemporary cognitive models (Abramowitz, Taylor, & McKay, 2009), such models are limited in that they ignore the importance of genetic factors and overemphasize the role of shared environment (Taylor & Jang, 2011). Although it is widely acknowledged that OC symptoms probably have a complex biopsychosocial etiology, to our knowledge there had been no previous attempt to integrate dysfunctional beliefs and genetic factors into a unified, empirically supported model. Based on a community sample of MZ and DZ twins who completed measures of dysfunctional beliefs and OC symptoms, we used structural equation modeling to compare three models: (a) The belief causation model, in which genetic and nonshared environmental factors influence beliefs and OC symptoms, and beliefs also influence symptoms, (b) the symptom causation model, which was the same as model (a) except that symptoms cause beliefs, and (c) the belief coeffect model, where beliefs and OC symptoms are the product of common genetic and environmental factors, and beliefs have no causal influence on symptoms. The belief causation model was the best fitting model. Beliefs accounted for a mean of 18% of phenotypic variance in OC symptoms. Genetic and environmental factors accounted, respectively, for an additional 36% and 47% of phenotypic variance. The best-fitting model obtained from these analyses appears in Fig. 3. The model describes an empirically supported integration of cognitive–behavioral and behavioral–genetic approaches. However, it is noteworthy that shared environment was not a significant component of this model and that dysfunctional beliefs accounted for only a small proportion (18%) of the variance in OC symptoms. Although the available findings offer a degree of support for some of etiologic variables proposed by cognitive–behavioral models (i.e., dysfunctional beliefs but not shared environment), these models are insufficient in part because they neglect the importance of genetic factors.

5. Summary and conclusions

Findings from this review indicated that (a) additive genetic effects and nonshared environment accounted for most of the variance in OC symptoms; (b) shared environment and nonadditive genetic effects made little or no contribution; (c) these findings did not vary with sex or symptom severity; (d) variance due to nonshared environment increased with age; (e) gene–environment interactions play an etiologic role; (f) OC symptoms are shaped by etiologic factors common to all types of OC symptoms but also have symptom-specific etiologies; and (g) OC symptoms are also shaped by very general etiologic factors (e.g., those influencing negative emotionality).

The conclusion that shared environment plays a limited role might seem at odds with studies suggesting that family environment plays an important role in OC symptoms (e.g., van Noppen & Steketee, 2009). The problem with such studies is that they failed to disentangle the effects of genes and shared environment. To illustrate, some studies suggest that parental rearing style and family emotional atmosphere (particularly parental overcontrol and criticism) are correlated with offspring OCD or OC symptom severity and course (van Noppen & Steketee, 2009; Waters & Barrett, 2000). The problem with such studies is that they fail to establish whether the effects are due to parental behavior (shared environment), parent–child reciprocal interactions (which could reflect gene-environment interactions), or whether the effects are simply due to shared genetic factors (e.g., genes regulating overcontrolling parenting styles might also play a role in offspring OC symptoms). Future research is needed to investigate whether, or how, parenting influences offspring OC symptoms.

OC symptoms have a complex etiologic architecture, which does not appear to be adequately captured by contemporary psychosocial or biological models. Part of the problem is that such models are typically reductionistic, in which the causes of OC symptoms are reduced to explanations based largely on either environmental effects (i.e., learning experiences) or hardwired biological factors (Abramowitz et al., 2009; Taylor et al., 2012). Cognitive–behavioral models overemphasize environmental variables, particularly shared environment, to the neglect of genetic factors. Contemporary biological models (reviewed in Abramowitz et al., 2009) overemphasize the role of hardwired (inherited) dysregulations in neurobiological circuitry, to the neglect of the role of environmental factors. Few, if any, contemporary models would have predicted, a priori, the complex etiologic architecture identified by twin studies, such as the nature of genetic and environmental factors, their hierarchy of specific and nonspecific etiological influences, and the genetic effects on OC-related dysfunctional beliefs. Twin studies highlight the need for comprehensive biopsychosocial models that are able to account for the etiological complexity revealed by empirical research.

Although twin studies indicate that genetic factors play an important role in OC symptoms, little is known about the specific genes that are involved. There have been many molecular genetic studies of OCD, but there have been a great many replication failures (Pauls, 2010). The nature of E also remains to be elucidated. That is, what kinds of nonshared environmental experiences are most likely to contribute to the development of OC symptoms? A number of studies have found that the onset of OC symptoms is associated with the onset of life stressors, such as job-related difficulties, becoming a new parent, or exposure to traumatic events (Abramowitz, Khandker, Nelson, Deacon, & Rygwall, 2006; Abramowitz, Nelson, Rygwall, & Khandker, 2007; Cromer, Schmidt, & Murphy, 2007; Millet et al., 2004). Further research is required to determine whether these events are causally related to OC symptoms or to OCD. Further research is also needed to better understand how genes and environmental factors interact to shape the development of OC symptoms, and how genes and the environment are moderated by age or other variables in the genesis and course of obsessions and compulsions.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.cpr.2011.09.008.

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