Behav Genet (2008) 38:108–120
DOI 10.1007/s10519-007-9185-9

ORIGINAL RESEARCH

Environmental Factors in Obsessive-Compulsive Behavior: Evidence from Discordant and Concordant Monozygotic Twins

Danielle C. Cath · Daniel S. van Grootheest · Gonneke Willemsen · Patricia van Oppen · Dorret I. Boomsma

Received: 9 May 2007 / Accepted: 12 November 2007 / Published online: 11 January 2008

Abstract To investigate environmental factors that protect against or exacerbate obsessive-compulsive (OC) symptoms, we selected 25 monozygotic (MZ) twin pairs discordant, 17 MZ twin pairs concordant high and 34 MZ pairs concordant low on OC symptoms from a large longitudinal Dutch sample of adult twin pairs and their family members, applying stringent criteria for OC symptomatology. Data were collected on psychopathology, family structure, health, lifestyle, birth complications and life events. Unique environmental factors were studied using within-discordant MZ pair comparisons, whereas between-concordant MZ pair comparisons were used to study environmental factors that are shared by the twins of an MZ pair. The high-scoring MZ twins of the discordant group reported more life events (especially sexual abuse) than their low-scoring twin-siblings. The between-pair comparisons showed lower birth weight in the discordant MZ pairs than in the concordant MZ pairs. Further, the concordant high MZ pairs as well as their spouses had a lower educational level than the two other groups. On scale scores of anxious-depression, neuroticism, and somatic complaints, concordant high MZ pairs showed highest scores, and the discordant MZ pairs scored intermediate, except for neuroticism, on which the high-scoring twins of discordant MZ pairs were equal to the concordant high pairs. Discordance on psychological scale scores between the concordant MZ pairs was evident from 1991 onward, and within the discordant MZ pairs from 1997 onward, confirming previous reports of an association of early-onset OC symptoms with higher genetic load. Parent scores of OC symptoms and anxious-depression suggested intermediate genetic load in the discordant MZ group. In conclusion, this study reports on both unique and shared environmental factors associated with OC symptomatology. Whether these factors operate in addition to or in interaction with genetic disposition is to be elucidated in future studies.

Keywords Monozygotic twins · Environmental factors · Life-events · Obsessive-compulsive symptoms · Discordant · Concordant

Introduction

Obsessive-compulsive disorder (OCD) is characterized by repetitive distressing and anxiety-provoking intrusive thoughts, mostly in combination with time-consuming repetitive actions designed to reduce tension or anxiety caused by the disturbing thoughts (American Psychiatric Association 1994). OCD can run, especially if untreated, a chronic and disabling course (Nestadt et al. 1998). Family studies have quite convincingly shown that early-onset OCD is familial (Pauls et al. 1995; Nestadt et al. 2000). Studies in 7- to 12-year-old twins have indicated that between 47 and 58% of the variance in obsessive-compulsive (OC) behavior is explained by additive genetic factors (Hudziak et al. 2004). The remaining variance is almost entirely explained by unique environment, with a small contribution of shared environmental factors (16%) at age 12. In adults, twin studies have indicated a more modest contribution of genetic factors (van Grootheest 2005 and others). One twin study in women suggested heritability of 33 and 26% respectively for obsessions and compulsions (Jonnal et al. 2000). Further, a recent twin

Edited by Tatiana Foroud.

D. C. Cath (✉) · D. S. van Grootheest · G. Willemsen · P. van Oppen · D. I. Boomsma
VU University Amsterdam, Amsterdam, The Netherlands
e-mail: dcath@xs4all.nl

study in 5,893 mono- and dizygotic twins, and 1,304 additional siblings from the population-based Netherlands Twin Register (NTR; Boomsma et al. 2002), indicated heritability estimates of 47% for both men and women (van Grootheest et al. 2007a, b).

The course of OCD is moderately stable: longitudinal twin studies as well as epidemiological and clinical studies have indicated that on average 50% of cases remit over time (van Grootheest et al. 2007a, b; Angst et al. 2004; Skoog and Skoog 1999). Environmental factors explain about half of persistence in boys and two-third of persistence in girls. Thus, environmental factors are of substantial importance in the likelihood to obtain and persist or remit with respect to OC symptomatology.

To date, only few studies have addressed the specific nature of these environmental factors in OC phenomenology. Which environmental influences can be detected from the literature? Family studies have revealed that parents of children with OCD suffer from poorer mental health and have fewer coping strategies than parents of healthy children (Derisley et al. 2005). A-specific risk factors for (the persistence of) OCD include: earlier age at onset, presence of co-morbid conditions and low socio-economic status (Skoog and Skoog 1999; Stewart et al. 2004, 2006; Angst et al. 2004). Further, OCD patients report more often than healthy controls to have been overprotected or emotionally neglected by their parents (Cavedo and Parker 1994). Patients with the hoarding subtype of OCD in particular, report a lack of parental emotional warmth (Alonso et al. 2004). Perinatal risk factors, such as prolonged labor and edema during pregnancy, have been reported to increase the risk of later OCD (Vasconcelos et al. 2007). Childhood sexual abuse appears to be an important mediator for later OCD, especially in women (Lochner et al. 2002). The relationship between religiosity and OCD is unclear. Some authors find increased frequencies of religious obsessions and hand washing among highly religious protestants in comparison with less or non-religious subjects (Abramowitz et al. 2004), while others find no relation between religiosity and an increase in OC symptoms (Assarian et al. 2006), and argue that religiosity is merely a form in which OC symptoms can be displayed (religious obsessions) (Tek and Ulug 2001). Finally, β-hemolytic streptococcal infections have been reported to be associated with OC symptom exacerbation (March et al. 1990).

The comparison of monozygotic (MZ) twins who score high on a trait with their low-scoring co-twins, comprises a powerful method to identify environmental factors involved in a disorder (Martin et al. 1997). MZ twins have identical genomes and are born and raised at the same time in the same family, thus sharing a very similar family environment. Consequently, discordance on the trait is mostly explained by differences in the non-shared (i.e., *unique*) environment that act either directly on the phenotype, or by epigenetic mechanisms (Fraga et al. 2005). Environmental factors that are *shared* by both members of a twin pair (such as maternal smoking during pregnancy, or parental divorce) can be studied by comparing MZ twins who are concordant high on the trait with MZ twins who are concordant low.

Comparisons within discordant MZ pairs or between concordant MZ pairs have not been employed to study environmental factors involved in OC phenomenology. In other psychiatric disorders, such as schizophrenia and ADHD (Stabenau and Pollin 1993; Lehn et al. 2007), as well as in somatic disorders such as diabetes mellitus (Bo et al. 2000), this method has been successfully used. One twin study on a disorder related to OCD, i.e., Gilles de la Tourettes' Syndrome, has studied basal ganglia D2-receptorbinding in five MZ twins who were discordant on tic severity, and found that caudate nucleus D2 receptor binding increased by up to 17% in the more severely affected twins when compared with their less severely affected twin siblings (Wolf et al. 1996). This within-MZ twin discordance reflects unique environmental influences on D2-caudate receptor density.

In this study, we used prospective data of adult twins from the NTR, who have been followed between 1991 and 2002, and about whom information on a wide range of variables was collected every 2–3 years (Boomsma et al. 2000). Differences between the MZ concordant and discordant groups were described using measures of anxiety and depression co-occurring with OC behavior. The aim of this explorative study was to replicate and extend the information from previous studies on both unique and shared environmental influences that might protect against or exacerbate OC behavior. Unique environmental factors were studied using within-discordant MZ twin pair comparisons. To study environmental factors shared by both twins of a pair, between-MZ pair comparisons were used. Parent data on level of education and on drinking and smoking behavior were used to compare the groups of twin pairs on these common environment influences. Further, measures of anxiety, depression and personality were compared between the parents of the concordant and discordant twin pairs, with the following reasoning: concordance between MZ twin pairs on OC behavior most likely results from genetic similarity between the twins of a pair. Thus, the contrasts between twin pairs who are concordant high and low reflect differences in genetic vulnerability to OC behavior. As a consequence, the parent scores on OC symptoms, on anxious depression and on neuroticism (the latter characteristics are known to be related to OC symptoms) are expected to reflect these differences in genetic vulnerability and therefore to be highest in the parents of the concordant high MZ pairs, to

be intermediate in the parents of the discordant MZ pairs and to be low in the parents of the concordant low MZ pairs.

Finally, longitudinal measures of psychopathology were studied to investigate age at onset of OC symptoms, anxiety and depressive symptoms in the concordant and discordant groups. Family studies have suggested that lower age at onset is associated with higher familiarity, possibly reflecting higher genetic load (Delorme 2005). We hypothesized that the concordant high MZ twin pairs, in whom the OC symptoms are theoretically more genetically determined, would show lower age at onset than the high-scoring twins of the discordant group in whom unique environmental factors might be more important.

Method

Sample selection

The data of this study originate from a longitudinal study in twin families registered with the NTR (Boomsma et al. 2002). Since 1991, twins and their families received a survey by mail every 2–3 years containing questionnaires about health, personality, life events, perinatal circumstances and lifestyle. The 2002 survey formed the starting point of this study. The Padua Inventory Abbreviated (PI ABBR) was added to the 2002 wave of data collection and was derived from the Padua Inventory-Revised version (PI-R), a widely used self-report inventory on OC symptoms (Sanavio 1988; van Oppen 1992). The PI-R is a 41-item self-report instrument that measures OC symptoms on a 0–4 scale, and contains five subscales: washing, checking, rumination, precision and impulses (van Oppen et al. 1995). It has been validated in the Netherlands, shows good psychometric qualities, and moderately correlates with the Y-BOCS symptom checklist, a clinician-derived checklist on OC symptoms (Denys et al. 2004). For the purpose of this epidemiological twin study, the PI-R was reduced to 12 items. Item choice was based on two items of each subscale with highest factor loadings in a previous validation study (van Oppen et al. 1995), and with one additional item for each of the more equivocal obsession subscales: rumination and impulses. The PI-R ABBR is shown in Table 1. To investigate its psychometric qualities psychometric analyses have been conducted in three groups derived from an earlier study by van Oppen et al. (1995). These groups encompassed a population-based control group ($n = 428$), a psychiatric control group ($n = 272$) and a clinical OCD group ($n = 120$); for an extensive description of the study groups (see van Oppen et al. 1995). Cronbachs' α of the scale was 0.73, which is an indication of good internal consistency. Analyses of variance (ANOVAs) of PI-R ABBR scores within the three groups revealed a significant main between-group effect ($p < 0.0001$). Post-hoc t-tests showed that the mean PI-R ABBR OC score for the OCD group (20.7 ± 8.1) was significantly higher than scores of the psychiatric control group (12.4 ± 7.4) as well as the population control group (6.6 ± 5.6; $p < 0.0001$ in both comparisons). To investigate whether the PI-R ABBR can accurately screen for OCD, and to establish cut-points of OC behavior, receiver operating characteristic (ROC) analyses were carried out. ROC analyses use the association between sensitivity and specificity to derive an area under the curve (AUC), which indicates how well a measure distinguishes between case positives (i.e., OCD group) and case negatives (i.e., psychiatric controls or population controls) irrespective of the base rate. A value of 0.50 of the AUC indicates chance level and 1.0 indicates a perfect diagnostic tool (Swets 1996; McFall and Treat 1999). The AUC for the PI-R ABBR when compared with clinical controls was 0.78 (95% CI = 0.73–0.83). When compared with the population controls, the AUC was 0.93 (95% CI = 0.90–0.95). At the best cut-off point of 16 (i.e., maximum difference between sensitivity and 1-specificity), the sensitivity was 0.74 with a specificity of 0.72, when compared with clinical controls. (A detailed description of the ROC analyses on the PI-R ABBR is available upon request through the first author.)

Of the adult twins, 2,672 pairs, their family members and–in some instances—their spouses (a total of 9,950 individuals) returned the survey. Monozygotic twin pairs were selected on the basis of high or low scores on the PI-R ABBR. Using the stringent criteria derived from the analyses described above, discordant, concordant high and concordant low MZ twin pairs were selected. Twin pairs were considered to be discordant when one twin scored >17 (in the clinical range), and his/her MZ twin sibling scored <7 (population control range). Pairs were considered to be concordant high when both twins scored >17, and concordant low when both twins scored <7. Information on zygosity from DNA polymorphisms was available in 19 MZ twin pairs (25%) of the final sample. When DNA polymorphisms were not available zygosity was determined from questions about physical similarity of the twins and confusion of the twins by family members, friends and strangers. Overall, agreement between zygosity diagnoses based on questionnaire and DNA data is 97% (Willemsen et al. 2005). After exclusion of incomplete pairs, 25 MZ discordant pairs, 17 MZ concordant high pairs and 521 MZ concordant low pairs were identified. Concordant low pairs were matched on age and sex with concordant high pairs and oversampled, so that 34 concordant low pairs were finally retained (Fig. 1).

Of the final 76 MZ twin pairs selected for this study, 18 pairs participated in wave 2002 only, 28 pairs participated

Table 1 The Padua Inventory-Revised abbreviated (PI-R ABBR)

	PI-R ABBR	Original factor
1	In certain situations, I am afraid of losing my self-control and doing embarrassing things	Impulses
2	I check and recheck gas and water taps and light switches after turning them off	Checking
3	I feel obliged to follow a particular order in dressing, undressing and washing myself	Precision
4	When I see a train approaching I sometimes think I could throw myself under its wheels	Impulses
5	I return home to check doors, windows, drawers etc., to make sure they are properly shut	Checking
6	When I start thinking of certain things, I become obsessed with them	Rumination
7	I feel I have to repeat certain numbers for no reason	Precision
8	Unpleasant thoughts come into my mind against my will and I cannot get rid of them	Rumination
9	My thoughts constantly go astray, therefore I find it difficult to attend to what is happening around me	Rumination
10	I sometimes have to wash or clean myself dimply because I think I may be dirty or 'contaminated'	Washing
11	I get upset and worried at the sight of knives, daggers and other pointed objects	Impulses
12	If I touch something which I think is 'contaminated', I immediately have to wash or clean myself	Washing

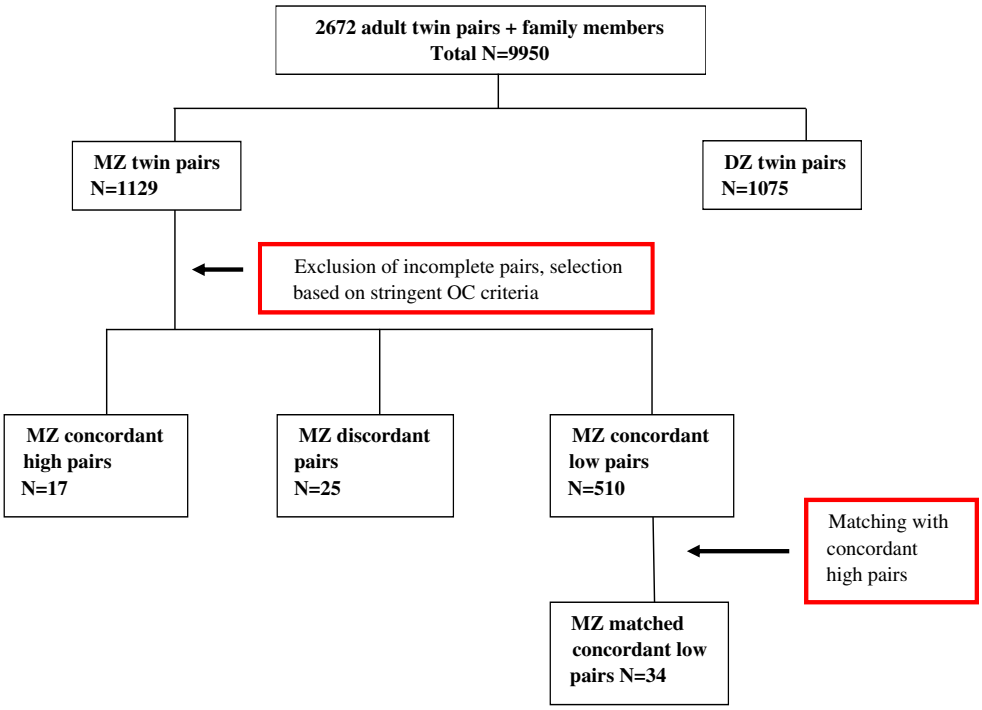

Fig. 1 The 2002 NTR wave using the PI-R abbreviated

in two waves, 4 pairs in three, 8 pairs in four, 13 pairs in five, and 4 pairs in all six waves.

Measures and instruments

The NTR survey contains a broad range of longitudinal measurements taken at six time points between 1991 and 2002, as well as cross-sectional measurements. Information is obtained on life events, perinatal adversities, physical and mental health, lifestyle factors such as physical activity, religiosity, drinking, smoking and drug behavior, and on demographic variables such as relationships, number of children, level of education, living situation, and work status. Since this is an exploratory study, all available information was taken into account.

Religiosity was assessed by asking whether the respondent had had a religious upbringing (yes/no), the person's current religion, and whether the respondent currently was an active church member.

On alcohol and smoking behavior, respondents were questioned about their consumption ever, in the past year and past month, as well as the number of cigarettes or glasses of alcohol per week. Alcohol dependence was assessed by the CAGE (four questions) (Bush et al. 1987).

The occurrence of negative life events throughout the lifespan was measured in the 2002 survey, using an adapted version of the Dutch life event scale (Schokverwerkings

Inventarisatie Lijst = SchIL) (van der Velden et al. 1992). This scale gathers information on: death of a spouse, father, mother, child, sibling or significant other; serious illness or injury of self or a significant other; divorce/break-up of a relationship; traffic accident; violent and sexual assault or rape, and robbery. Response categories are: never experienced; 0–6 months ago; 6–12 months ago; 1–5 years ago, and more than 5 years ago.

Data on anxiety and depression were available at most time points between wave 1 and 6, and were assessed with: the Spielberger State-Trait Anxiety Inventory, trait scale (Spielberger et al. 1970; van der Ploeg 1979), and the young adult self-report (YASR), anxious-depressed subscale (Achenbach 2000; Verhulst et al. 1997). Questionnaires between waves 1 and 4 (between 1991 and 1997) also contained the 8-item OC symptom subscale of the YASR (Nelson et al. 2001; Geller et al. 2006). Neuroticism, somatic complaints and extraversion were measured with the Amsterdamse Biografische Vragenlijst (ABV; Amsterdam Biographical Questionnaire) (Wilde 1970). The ABV neuroticism and extraversion scales are very similar to the Eysenck Personality Questionnaire neuroticism and extraversion subscales (Eysenck and Eysenck 1964), and contain answer categories: yes/no/don't know. The satisfaction with life scale and the subjective happiness scale (Lewis and Joseph 1995), a combined 10-item scale with scoring possibilities between 1 and 7 were taken, and the Rosenberg self-efficacy scale, a 10-item scale scoring between 1 and 4 (Rosenberg 1965; Helbing 1982).

Socio Economic Status (SES) in 2002 was assessed using a full description of the occupation of the twins according to the descriptions provided by the Central Office for Statistics in the Netherlands. The work level was coded into three levels based on the mental complexity of the work, ranging from low skilled (1) to academic work (3). Living situation was coded between 1 and 3 (1 = with parents; 2 = alone; 3 = with partner).

Finally, we used child-derived information on their parents' level of education. Direct parent information was used to collect information on their smoking and drinking behavior and on their scores of OC behavior, anxiety and depression.

Statistical analyses

Within-pair analyses

Within-discordant pair differences between the high and low-scoring twins on the PI-R ABBR were calculated using paired *t*-tests (*t*-tests for two related samples) for continuous data, Wilcoxon signed- rank tests for ordinal data and McNemar χ^2 tests of matched pairs for nominal data.

Between-pair analyses

Variables that measure psychological health, as well as measures of environmental influences on OC symptoms were compared between the concordant high, the concordant low and the discordant MZ twin pairs, using one-way ANOVAs for continuous data, Kruskal–Wallis tests for ordinal data and χ^2 tests for nominal data. Post hoc comparisons were conducted using post hoc Scheffé's (continuous data) and Mann–Whitney *U*-tests (ordinal data). Post hoc Scheffé testing, although more liberal than Bonferroni correction, provide some correction of type I error. Two-tailed probabilities were used in all analyses, since we had no clear expectation of the direction of the findings.

To adjust for correlated error in the between-group comparisons of common environment variables, separate regression analyses (multiple regression for continuous measures and logistic regression for categorical measures) were conducted in STATA 9.2 for these variables (StatCorp, College Station, TX, USA). The robust cluster option was used to account for nonindependence of the twin pairs on the variables that reflected common environmental influences (i.e., caesarean section, birth weight, and religious upbringing of the twin; parental death and divorce, death of a sibling, and level of education, alcohol use and smoking behavior of the parents). Alpha was set at 0.05.

Results

Within-pair analyses of discordant pairs

Twenty-five MZ twin pairs discordant on OC behavior were included, of whom 18 pairs were female. Their mean age was 29.6 years (SD 6.8 years). Mean PI-R ABBR OC scores in the high-scoring twins of the discordant pairs were 21.4 (SD 5.9), in the low scoring twins 4.5 (SD 2.0).

Health and lifestyle characteristics

High-scoring twins of the discordant pairs experienced lower general health ($p = 0.03$) and more impediments in physical activity ($p < 0.001$) than the low-scoring co-twins. The duration of the current relationship of the high-scoring twins tended to be shorter ($p = 0.06$), and they tended to have fewer children ($p = 0.07$). They were less satisfied with life ($p = 0.02$), less happy ($p = 0.001$) and had lower self-efficacy scores ($p = 0.006$). They showed no differences with respect to birth weight, birth order, church participation, drinking or smoking behavior, nor on level of education, work status, living situation, or number

of (mental) health contacts. The high-scoring twins of the discordant pairs scored significantly higher on the YASR anxious-depressed subscale ($p < 0.001$), on the neuroticism subscale ($p < 0.001$), on the ABV subscale of somatic complaints ($p < 0.001$), and on STAI-trait ($p < 0.001$). On the ABV extraversion scale, no within-pair differences were found (Table 2).

Unique environment influences

The only within-pair difference found on unique life events, was the tendency of the high-scoring twins of the discordant pairs to have experienced more sexual assault than the low-scoring twins ($p = 0.08$). All persons who had experienced sexual assault were women. Two low-scoring twins of the discordant pairs reported on sexual assault, versus five high-scoring twins. The low-scoring twins and four of the five high-scoring twins of the discordant pairs reported to have experienced the assault more than 5 years ago, versus one twin who had experienced sexual abuse between 1 and 5 years ago (Table 3).

Longitudinal data

Young adult self-report OC subscale scores, taken in 1991, 1995 and 1997, revealed significant differences between high and low-scoring twins of the discordant pairs in 1997 ($p = 0.007$). Further, scale scores between 1991 and 2002 revealed significant within-pair differences on the YASR anxious-depressed subscale from 1997 onward ($p = 0.001$), on the neuroticism subscale from 1993 onward (p-value between 0.01 and <0.001 at wave 2–5), on the ABV subscale of somatic complaints from 1997 onward (p-value between 0.015 and <0.001), and on STAI-trait scores from 1997 onward (p-values between 0.007 and <0.001).

Between-pair analyses of concordant and discordant pairs

Seventeen MZ twin pairs were included who were concordant high on OC behavior, of whom 14 pairs were female. Their mean age was 30.0 years (SD 11.2 years), mean PI-R ABBR OC scores were 23.7 (SD 6.7). Thirty-four MZ twin

Table 2 2002 wave of data collection: within-discordant twin pair characteristics

	Low risk twin, mean (SD)	High risk twin, mean (SD)	Test statistic*	p-Value
Birth weight (g)	2,189 (806)	2,028 (667)	0.9	n.s.
Birth order (first born)	$n = 10$	$n = 14$	1.7	n.s.
General health (1–5)	4.1 (0.7)	3.8 (0.6)	2.3	0.03
Mental health contacts ever yes	$n = 7$	$n = 9$	0.5	n.s.
Sumscore impediments physical activity	43.5 (12.5)	53.9 (12.4)	−4.2	<0.001
Number of persons drinking ever	$n = 23$	$n = 23$	0	n.s.
Number of drinks per week (past 12 months)	11.1 (1.4)	13.4 (0.7)	0.19	n.s.
CAGE score alcohol dependence	4.0 (0.2)	4.3 (0.7)	−1.4	n.s.
Duration current relation (years)	5.9 (7.4)	3.0 (0)	1.97	n.s.
Number of children	1.1 (1.2)	0.7 (0.6)	1.87	n.s.
Education level self (1–13)	7.9 (3.0)	8.3 (2.6)	−0.8	n.s.
Education level partner (1–13)	8.3 (3.6)	8.1 (3.1)	−1.2	n.s.
Living situation (1–4)	2.8 (0.8)	2.7 (0.8)	−1.3	n.s.
PI-R ABBR OC scale	4.5 (2.0)	21.4 (5.9)	−13.7	<0.001
YASR anxious depression scale	4.3 (2.8)	11.6 (4.3)	−6.4	<0.001
ABV extraversion	51.0 (16.7)	45.6 (12.5)	1.1	n.s.
ABV neuroticism	48.6 (23.1)	85.3 (27.4)	−5.8	<0.001
ABV somatic complaints	16.6 (5.1)	24.4 (10.3)	−4.0	<0.001
STAI-trait	31.6 (4.7)	46.4 (10.8)	−6.5	<0.001
Satisfaction with life scale scores	27.4 (4.1)	23.8 (7.0)	2.3	0.02
Happiness scores	22.7 (3.9)	17.9 (5.8)	23	0.001
Self-efficacy scores	31.3 (4.0)	27.5 (4.7)	2.9	0.006

PI-R ABBR, Padua Inventory-Revised Abbreviated; OC, obsessive-compulsive; YASR, young adult self-report; ABV, Amsterdamse Biografische vragenlijst; STAI, State trait Anxiety Inventory; SBL, Spannings behoefte Lijst (sensation seeking list); CI, confidence interval; n.s., not significant

Table 3 Within-discordant twin comparisons—unique life events

	Low OC twin, mean (SD)	High OC twin, mean (SD)	*p*-Value
Birth weight (g)	2,189 (806)	2,028 (667)	n.s.
Disease self (0–2)	0.08 (0.4)	0.26 (0.6)	n.s.
Disease child (0–2)	0.09 (0.4)	0.6 (0.1)	n.s.
Disease partner (0–2)	0.09 (0.4)	0	n.s.
Disease significant other (0–2)	0.82 (0.9)	0.82 (0.9)	n.s.
Death child (0–2)	0	0	n.s.
Death partner (0–2)	0	0	n.s.
Death significant other (0–2)	1.1 (0.9)	1.0 (0.9)	n.s.
Sexual abuse* (0–2)	0.17 (0.5)	0.43 (0.8)	0.08
Violence (0–2)	0.17 (0.6)	0.17 (0.6)	n.s.
Relationship termination (0–2)	0.52 (0.8)	0.82 (0.9)	n.s.
Theft (0–2)	0.47 (0.8)	0.56 (0.8)	n.s.
Traffic accident (0–2)	0.52 (0.8)	0.38 (0.7)	n.s.
Dismissal (0–2)	0.30 (0.7)	0.48 (0.7)	n.s.
Total score life events	2.35 (1.9)	2.76 (1.7)	n.s.

pairs were included who were concordant low on OC behavior, of whom 28 pairs were female. Their mean age was 30.0 years (SD 11.3 years), mean PI-R ABBR OC scores were 3.8 (SD 2.2).

Health and lifestyle characteristics

The concordant low group generally experienced the best health, with the discordant group scoring intermediate between high and low concordant groups. Members of the discordant group more often had a spouse than the concordant high group, and were living with a spouse more often than both concordant groups. No between-group differences were found for smoking behavior. For drinking behavior, the concordant high group showed the highest scores on alcohol dependence ($p = 0.02$ and 0.04 in comparison with the concordant low and discordant group), although they scored intermediate between the low and discordant groups on current number of drinks per week. On religious upbringing, there were no significant differences between the study groups. Interestingly, the concordant low MZ twin pairs, as well as their spouses, reported to have a higher level of education than the concordant high and discordant twin pairs (*p*-values 0.02 in both comparisons) (Table 4).

On life events, the concordant high MZ twin pairs reported more often that they had been dismissed from work than the concordant low scoring pairs ($p = 0.04$), with the discordant pairs scoring between the concordant high and low pairs. Further, the discordant pairs reported more often to have been sexually assaulted in comparison with both the concordant low and high-scoring pairs; $n = 7$ individuals in the discordant group versus $n = 0$ and $n = 1$ individual in the concordant high and low groups ($p = 0.02$ and 0.03 respectively). Finally, the discordant pairs reported more traffic accidents than the other groups ($p = 0.05$ and 0.02 when compared with the concordant low and high pairs respectively).

On psychological scale scores, the concordant high group scored, as expected, overall higher on the PI-R-ABBR (*p*-values <0.001), the YASR anxious-depressed scale (*p*-values <0.001), ABV neuroticism ($p < 0.001$ in low–high comparison; p = n.s. between high and discordant twin pairs), somatic complaints (*p*-values between <0.001 and 0.003), and STAI-trait anxiety (*p*-values <0.001). Further, the concordant high group had lower scores on ABV extraversion (*p*-values 0.001), satisfaction with life (*p*-values between 0.01 and 0.001), happiness (*p*-values between 0.01 and <0.001) and self-efficacy (*p*-values <0.001) than the concordant low and discordant groups.

Shared environment influences

Between-group analyses revealed that the discordant group had the lowest rate of caesarean sections (*p*-values of 0.005 and 0.006 in comparison with the concordant low and high groups), while there was no difference between the concordant groups. The discordant group had the lowest birth weight ($p = 0.008$ compared with the concordant low pairs and $p < 0.001$ compared with the concordant high pairs). There were no between-group differences on level of education of the parents (*p*-values = n.s. in all comparisons). There were no between-pair differences in the occurrence of parental death. The concordant low MZ pairs reported most on death of a sibling ($p = 0.05$ between concordant low and high pairs). There were no between-

Table 4 2002 wave of data collection: between concordant and discordant twin pair health and lifestyle characteristics

	Concordant Low twin pairs, mean (SD)	Concordant high twin pairs, mean (SD)	Discordant twin pairs, mean (SD)	Low–high *p*-value	Low–discordant *p*-value	High–discordant *p*-value
General health (1–5)	4.4 (0.7)	3.6 (1.2)	4.1 (0.7)	<0.001	0.007	n.s.
Mental health contacts ever yes	$n = 8$ (12%)	$n = 21$ (61%)	$n = 16$ (32%)	<0.001	0.006	0.009
Impediments physical activity	41.3 (12.6)	53.0 (17.1)	43.5 (12.5)	0.001	n.s.	0.03
Specialized medical treatment ever yes	$n = 11$ (16%)	$n = 15$ (44%)	$n = 11$ (22%)	0.002	n.s.	0.04
Currently active in church (1–3)	0.8 (0.7)	0.5 (0.7)	0.9 (0.8)	n.s.	n.s.	n.s.
Number of persons drinking ever	$n = 62$ (91%)	$n = 19$ (56%)	$n = 35$ (70%)	n.s.	0.003	n.s.
Number of drinks per week (past 12 months)	2.7 (1.4)	2.3 (1.5)	1.9 (1.2)	n.s.	0.01	n.s.
CAGE score alcohol dependence	4.1 (0.5)	4.5 (0.8)	4.2 (0.5)	0.02	n.s.	0.04
Number of persons smoking ever	$n = 20$ (29%)	$n = 14$ (41%)	$n = 18$ (36%)	n.s.	n.s.	n.s.
Number of cigarettes per day (1–7)	4.1 (1.1)	4.7 (1.1)	3.8 (1.0)	n.s	n.s.	0.07
Number of persons with partner	$n = 41$ (60%)	$n = 17$ (50%)	$n = 35$ (70%)	n.s.	n.s.	0.04
Children yes	$n = 16$ (23%)	$n = 8$ (23%)	$n = 25$ (50%)	n.s.	0.003	0.015
Education level self (1–13)	9.4 (2.3)	8.27 (2.8)	8.24 (2.8)	0.02	0.02	n.s.
Education level partner (1–13)	9.1 (2.8)	6.7 (3.7)	8.20 (3.4)	0.006	n.s.	n.s.
Living situation (1–3)	2.4 (0.8)	2.2 (1.0)	2.8 (0.8)	n.s.	0.04	0.01
PI-R ABBR OC scale	3.8 (2.2)	23.7 (6.7)	12.9 (9.5)	<0.001	<0.001	<0.001
YASR anxious depression scale	2.9 (4.7)	14.5 (19.3)	8.7 (12.6)	<0.001	<0.001	<0.001
ABV extraversion	62.8 (16.2)	46.4 (17.7)	48.3 (17.7)	<0.001	<0.001	0.001
ABV neuroticism	36.2 (18.9)	92.8 (19.7)	66.6 (31.1)	<0.001	<0.001	n.s.
ABV somatic complaints	15.7 (3.7)	27.5 (8.3)	20.3 (8.8)	<0.001	0.003	<0.001
STAI-trait	29.4 (6.4)	36.9 (7.9)	37.6 (7.5)	<0.001	<0.001	<0.001
Satisfaction with life	28.7 (4.0)	19.8 (7.2)	25.6 (5.9)	<0.001	0.01	0.001
Happiness	24.2 (3.2)	16.2 (5.7)	20.4 (5.4)	<0.001	<0.001	0.01
Self-efficacy	33.7 (3.9)	25.5 (3.9)	29.4 (4.7)	<0.001	<0.001	<0.001

group differences with respect to relationship termination of the parents. On both drinking and smoking behavior of the parents, surprisingly the concordant low parents reported more drinking than the discordant parents, although alcohol consumption as well as number of cigarettes were low on average (Table 5).

Longitudinal data

Young adult self-report OC scale scores revealed significant differences between low and high-scoring twin pairs in the 1995 ($p = 0.02$) and 1997 wave ($p < 0.001$). YASR anxious-depressed scale scores revealed significant differences between the concordant low and high groups from 1991 on (p-values < 0.05 in all comparisons). ABV extraversion scores revealed significant between-group differences from 1993 onward (p-values between <0.001 and 0.008), whereas ABV neuroticism scores revealed significant between-group differences at all waves (p-values between 0.05 and <0.001). ABV somatic complaints showed significant between-group differences from 1997 on (p-values <0.001).

Parent data

Parent data were available for 66 persons; the 34 parents of concordant low twin pairs had a mean age of 53.6 years (SD 5.9), a PI-R ABBR mean score of 5.2 (SD 3.8); 9 parents of concordant high twin pairs had a mean age of 51.6 years (SD 2.5), and a PI-R ABBR mean score of 11.7 (SD 3.8); and 23 parents of discordant twin pairs had a mean age of 57.5 years (SD 6.9) and a PI-R ABBR mean score of 9.9 (SD 5.7). Between-group analyses of psychological scale scores showed that the parents of the discordant pairs scored between the parents of the concordant low and high pairs on anxious depression, satisfaction with life, happiness and self-efficacy scales. On somatic complaints and extraversion they showed higher

Table 5 Between twin-pair comparisons: comparison of common environment characteristics (after correction for interrelatedness)

	Concordant low twin pairs, mean (SD)	Concordant high twin pairs, mean (SD)	Discordant twin pairs, mean (SD)	Low–high *p*-value	Low–discordant *p*-value	High–discordant *p*-value
Caesarean section (yes)	$n = 5$ pairs	$n = 3$ pairs	$n = 0$ pairs	n.s.	0.008	<0.001
Birth weight (g)	2,650 (876)	2,685 (795)	2,109 (736)	n.s.	0.004	0.009
Religious upbringing yes	$n = 45$ (67%)	$n = 16$ (47%)	$n = 34$ (69%)	n.s.	n.s.	n.s.
Education level father[a] (1–13)	7.5 (4.0)	5.5 (3.7)	5.7 (3.5)	n.s.	n.s.	n.s.
Education level mother[a] (1–13)	6.3 (3.7)	5.2 (3.4)	4.7 (3.0)	n.s.	n.s.	n.s.
Death mother (0–2) yes	$n = 2$ (3%)	$n = 3$ (10%)	$n = 4$ (8%)	n.s.	n.s.	n.s.
Death father (0–2)	$n = 12$ (19%)	$n = 7$ (24%)	$n = 6$ (12%)	n.s.	n.s.	n.s.
Death sibling (0–2)	$n = 6$ (10%)	$n = 0$	$n = 1$ (2%)	0.05	n.s.	n.s.
Relationship termination parents (0–2)[b]	$n = 4$ (14%)	$n = 2$ (25%)	$n = 1$ (7%)	n.s.	n.s.	n.s.
Number of parents drinking (ever; yes)[b]	91%	100%	74%	0.06	n.s.	0.04
Number of drinks/week parents (1–7)[b]	3.5 (4 drinks/week)	2.7 (2–3 drinks/week)	2.3 (1–2 drinks/week)	n.s.	0.03	n.s.
Number of parents smoking ever (yes)[b]	71%	89%	48%	n.s.	0.06	0.07
Number of cigarettes/day parents (1–7)[b]	4 (6–10 cig/day)	5(11–20 cig/day)	5 (11–20 cig/day)	n.s	n.s.	n.s.

[a] Reported by twin children and by parents

[b] Direct parent data

scores than the other groups. On the PI-R ABBR, STAI trait and neuroticism they scored equal to the parents of the concordant high groups (Table 6).

Discussion

The most important aim of this MZ twin study has been to explore unique and shared environmental factors involved in OC symptoms.

Unique and shared environmental factors

The within-twin pair comparisons of the MZ discordant pairs were primarily used to study *unique* environmental factors associated with OC symptoms. Although the discordant pairs were genetically identical, were raised at the same time in the same family, and were selected from an epidemiological sample, the twins differed substantially on several measures across time. The twins who scored low on OC symptoms reported to feel healthier, to be more

Table 6 2002 wave of data collection: between-parents comparisons of psychological scales

	Parent concordant low, mean (SD)	Parent concordant high, mean (SD)	Parent discordant, mean (SD)	High–low *p*-value	Low–discordant *p*-value	High–discordant *p*-value
PI-R ABBR OC scale	5.2 (3.8)	11.7 (3.8)	9.9 (5.7)	0.002	0.002	n.s.
YASR anxious depression scale	4.5 (3.5)	11.7 (4.2)	7.7 (4.3)	<0.001	0.02	0.04
ABV extraversion	53.4 (17.5)	44.9 (12.9	62.4 (13.3)	n.s.	n.s.	0.02
ABV neuroticism	36.3 (25.3)	79.8 (26.5)	62.7 (13.3)	<0.001	<0.001	n.s.
ABV somatic complaints	16.3 (4.5)	21.2 (6.6)	26.9 (2.3)	0.01	<0.001	0.005
STAI-trait	29.5 (6.7)	44.1 (7.1)	47.7 (4.1)	<0.001	<0.001	n.s.
Satisfaction with life	28.1 (4.9)	18.6 (8.5)	25.5 (7.1)	0.001	n.s.	0.03
Happiness	23.5 (3.5)	16.3 (6.9)	15.1 (3.3)	<0.001	<0.001	n.s.
Self-efficacy	32.1 (3.8)	28.0 (4.2)	25.3 (2.6)	0.01	<0.001	n.s.

PI-R ABBR, Padua Invetroy-Revised Abbreviated scale; OC, obsessive-compulsive; YASR, young adult self-report; ABV, Amsterdamse Biografische vragenlijst; STAI, State trait Inventory

satisfied with life, happier and more self-efficient than their high scoring MZ twin siblings. They tended to have longer relationships and more children. Further, they had lower scores on anxious depression and on neuroticism, mostly from 1997 onward. The most striking unique environmental factor to explain these within-discordant pair differences was the relatively high frequency of sexual assault experienced by the high-scoring twins of the discordant pairs in comparison with their low-scoring twin siblings, which is in line with previous reports on this issue (Lochner et al. 2004). However, two of the low-scoring twins of the discordant pairs reported on sexual assault as well, underscoring the complexity of presumed causality in the interplay between environmental and genetic factors in OCD. Interestingly, no sexual assault was reported by the concordant high-scoring MZ twin pairs. Thus, although the high-scoring respondents of the discordant pairs show similar OC symptomatology when compared with the concordant high MZ pairs, the pathways along which similar OC symptoms develop seem to differ between the high-scoring discordant twins on the one hand, and the high-scoring concordant pairs on the other. Although one can only speculate about causal relationships in this explorative study, the OC symptoms in the high-scoring twins of the discordant pairs seem to be associated more with environmental stressors (i.e., sexual assault) than are the OC symptoms in the concordant high-scoring pairs.

The between-twin pair comparisons to study environmental factors that are *shared* by the twins of a pair revealed low birth weight and low rates of caesarean section in the discordant pairs. We were unable to take the relationship between low birth weight and gestational age into account in the analyses, and were therefore unable to distinguish whether the study persons had been pre- or dysmature at birth. However, a recent twin study showed that low birth weight in itself resulted in an increase in problem behavior in later life. Children with low birth weight appeared to be more vulnerable to negative environmental factors than normal birth weight children (Wichers et al. 2002), possibly in association with a negative interaction between genetic vulnerability for problem behavior and low birth weight. Low birth weight can be indicative of a range of prenatal adversities such as maternal psychological stress, alcohol, drug abuse, or smoking during pregnancy. These adversities cause immunological challenge, and lead through various mechanisms to a diversity of psychopathology, including anxiety and depression (Meyer et al. 2006; Huizink et al. 2004; Nigg and Breslau 2007). In this study, we did not find an indication of alcohol, smoking or drug abuse in the parents of the twin pairs, but other sources of prenatal stress can not be ruled out. Further, no discordant twin pairs were born through caesarean section, as opposed to eight concordant pairs. This is remarkable in light of the fact that in general, caesarean section is carried out more often in multiple pregnancies, especially when one suspects low birth weight in the fetuses (Colla et al. 2001). Although it might be a chance finding, one can speculate that—since caesarean section is intended to decrease perinatal adversities—the discordant group of this sample has been 'under treated', providing an additional negative environmental factor to explain between-group differences.

There were no between-group differences in rates of parental death or death of a sibling, nor in frequency of relationship termination between the parents, life events that reflect shared environmental stressors. In general, rates of these life events were low in this relatively young twin group, possibly hampering detection of between-twin pair differences. Alcohol use by the mother (especially during pregnancy) as well as maternal smoking are considered to be common environmental risk factors for problem behavior such as ADHD (Smidts 2007). However, neither alcohol use nor smoking behavior of the parents was associated with OC symptoms in the concordant high or discordant groups of this study. Further, there was no association between OC symptoms and a religious upbringing in the study groups, which is in line with the literature on the lack of association between religiosity and OCD (Tek et al. 2004), but deviates from reports of a protective effect of religion on other forms of psychopathology such as alcohol and drug abuse, depression and disruptive behavior (Kendler et al. 1999). Apparently, different problem behavior is associated with different environmental risk factors.

Finally, level of education of the parents (as a measure of socio-economic status, a risk factor reported in OCD) was not found to be associated with OC symptoms in this study, although the parents of the twins who were concordant low on OC symptoms tended to have a higher level of education than the other groups, a difference that may have failed to reach significance due to the small sample size.

Finally, between-twin pair comparisons on unique life events revealed an elevated rate of dismissal in the concordant high-scoring twin pairs compared with the other pairs. Since dismissal typically represents a unique negative environmental influence on each twin of a pair, instead of being an environmental influence shared between the twins of a pair, its elevated rate among the high-scoring concordant MZ pairs is better explained as being the consequence of OC symptomatology rather than causing OC symptoms; elevated dismissal rates in these OC twin pairs might result from over-scrupulosity and slowness in work—characteristics well known in OC symptomatology—and subsequent dysfunction.

Health and lifestyle characteristics

Overall, as expected, the concordant low pairs reported highest scores of health, fewest mental and medical health contacts, and lowest scores on OC symptoms, anxiety and depression, neuroticism, and somatic complaints compared with the other groups. Further, they reported to be more extravert, more satisfied with life, happier and more self-efficient, with the discordant pairs scoring in between the concordant low and high pairs. On alcohol use, the concordant high-scoring twin pairs scored in between the low and discordant twin pairs over the past 12 months, with the number of drinks per week well below the quantity required to fulfil criteria for alcohol abuse or dependence according to DSM-IV criteria. However, subjective reports of alcohol withdrawal and dependence (CAGE scores) were increased in the high-scoring twin pairs compared with the low-scoring and discordant pairs. This might reflect increased scrupulosity and feelings of guilt, a well-known phenomenon in persons with OC symptoms, (Olatunji et al. 2006), related to alcohol use and its toxic effects rather than a verifiable alcohol problem in the concordant high-scoring MZ pairs.

A protective effect of level of education on OC symptoms was suggested by the finding of a higher level of education in the concordant low-scoring twin pairs than in the concordant high and the discordant twin pairs. Not only the concordant high-scoring twin pairs but also their spouses had a lower level of education, which suggests that low level of education and OC symptomatology might share genetic vulnerability. Deficits in encoding complex information and subsequent memory impairments have been reported in OCD (Buhlmann et al. 2006; Deckersbach et al. 2000). These (genetically determined) impairments possibly mediate low educational level. On the other hand, low level of education in the concordant high-scoring group might be a consequence of the OC symptomatology in itself, a notion that is supported by the literature (Sorensen et al. 2004).

The longitudinal data

As expected, the longitudinal data on OC symptoms, anxiety and depressive symptoms in the concordant and discordant groups revealed an earlier age at onset of OC and related symptoms in the concordant high group (from 1991 on) than in the discordant group (mostly from 1997 on). This confirms data from family-based studies where an earlier age at onset was associated with higher familial load (do Rosario-Campos et al. 2005). Thus, assuming that OC symptoms in the concordant high-scoring twin pairs are more genetically mediated than in the discordant pairs, this study is in line with clinical studies indicating that age at onset might be an important phenotypic characteristic that reflects differences in genetic characteristics underlying OCD (Delorme et al. 2005).

The parent data

As parent scores on OC symptoms and related psychopathology were expected to reflect genetic vulnerability, we expected scores to be highest in the concordant high parents, to be intermediate in the discordant parents and to be low in the concordant low parents. On most measures of psychopathology, this assumption was confirmed. Thus, the intermediate scores in the parents of the discordant twins on OC, anxious-depression and neuroticism scales may be the consequence of the intermediate amount of genetic vulnerability to OC symptoms in this group. Therefore, these parent data suggest that the symptoms in the high-scoring twins of the MZ discordant group are likely to be the consequence of a moderate genetic vulnerability to OC pathology in addition to or in interaction with environmental mediators.

Limitations

First, sample size is small; although we sampled from a large group of MZ twins, only a small sample was retained due to the use of rigorous criteria. Consequently, especially in the within-discordant pair comparisons, some of the negative outcomes might in fact be the result of lack of power to detect within-pair differences. Alternatively we could have relaxed the stringent selection criteria, with the disadvantage of including twin pairs not scoring in the clinical range of OCD, thus representing an unclear group of problem behavior.

Second, considering the large number of tests relative to the small sample size, we only mildly corrected for type I errors. However, considering the exploratory nature of this study, an increase in the odds of type II errors by correction of type I errors was undesirable. Therefore, we decided to compromise by only applying a mild correction of type I errors (Perneger 1998).

Finally, the database used in this study was not primarily designed to specifically inquire about environmental factors, leaving some questions unanswered, especially with respect to protective environmental mediators of OC symptomatology.

Conclusion

This study has been a first attempt to identify characteristics of the environment associated with OC symptoms

using a twin study design. Some important environmental factors involved in OC symptomatology have been identified. Two crucial questions to be addressed in future studies are: (1) what is the differential impact of the various environmental mediators on OC symptoms, and under which circumstances and at which age are they most harmful? (2) Along which lines do the environmental factors found in this study operate? Do they add to genetic risk factors, are they causal in themselves, or do they operate through gene–environment interaction? Future studies are needed to study the differential effects of environment and genes on phenotypes (and endophenotypes), and to elucidate the nature of the interplay between genes and environment.

References

Abramowitz JS, Deacon BJ, Woods CM, Tolin DF (2004) Association between protestant religiosity and obsessive-compulsive symptoms and cognitions. Depress Anxiety 20:70–76

Achenbach TM (2000) The young adult self report. University of Vermont, Dept of Psychiatry, Burlington

Alonso P, Menchon JM, Mataix-Cols D, Pifarre J, Urretavizcaya M, Crespo JM, Jimenez S, Vallejo G, Vallejo J (2004) Perceived parental rearing style in obsessive-compulsive disorder: relation to symptom dimensions. Psychiatry Res 127:267–278

American Psychiatric Association (1994) In: Williams JBW, Spitzer RL (eds) Diagnostic and statistical manual of mental disorders, 4th edn. American Psychiatric Press, Washington DC

Angst J, Gamma A, Endrass J, Goodwin R, Ajdacic V, Eich D, Rossler W (2004) Obsessive-compulsive severity spectrum in the community: prevalence, comorbidity, and course. Eur Arch Psychiatry Clin Neurosci 254:156–164

Assarian F, Biqam H, Asqarnejad A (2006) An epidemiological study of obsessive-compulsive disorder among high school students and its relationship with religious attitudes. Arch Iran Med 9:104–107

Bo S, Cavallo-Perin P, Scaglione L, Ciccone G, Pagano G (2000) Low birthweight and metabolic abnormalities in twins with increased susceptibility to Type 2 diabetes mellitus. Diabet Med 17:365–370

Boomsma DI, de Geus EJ, Van Baal GC, Koopmans JR (1999) A religious upbringing reduces the influence of genetic factors on disinhibition: evidence for interaction between genotype and environment on personality Twin Res 2:115–125

Boomsma DI, Beem AL, van den Berg BM, Dolan CV, Koopmans JR, Vink JM, de Geus EJ, Slagboom PE (2000) Netherlands twin family study of anxious depression (NETSAD). Twin Res 3:323–334

Boomsma DI, Vink JM, Van Beijsterveldt TC, de Geus EJ, Beem AL, Mulder EJ, Derks EM, Riese H, Willemsen GA, Bartels M, van den Berg BM, Kupper NH, Polderman TJ, Posthuma D, Rietveld MJ, Stubbe JH, Knol LI, Stroet T, van Baal GC (2002) Netherlands twin register: a focus on longitudinal research. Twin Res 5:401–406

Buhlmann U, Deckersbach T, Engelhard I, Cook LM, Rauch SL, Kathmann N, Wilhelm S, Savage CR (2006) Cognitive retraining for organizational impairment in obsessive-compulsive disorder. Psychiatry Res 144:109–116

Bush B, Shaw S, Cleary P, Delbanco TL, Aronson MD (1987) Screening for alcohol abuse using the CAGE questionnaire. Am J Med 82:231–235

Cavedo LC, Parker G (1994) Parental bonding instrument. Exploring for links between scores and obsessionality. Soc Psychiatry Psychiatr Epidemiol 29:78–82

Chabane N, Delorme R, Millet B, Mouren MC, Leboyer M, Pauls D (2005) Early-onset obsessive-compulsive disorder: a subgroup with a specific clinical and familial pattern? J Child Psychol Psychiatry 46:881–887

Clifford CA, Murray RM, Fulker DW (1984) Genetic and environmental influences on obsessional traits and symptoms. Psychol Med 14:791–800

Colla F, D'Addato F, Grio R (2001) Delivery in multiple pregnancies Minerva. Ginecol 53:101–105

de Geus EJ, van 't Ent D, Wolfensberger SP, Heutink P, Hoogendijk WJ, Boomsma DI, Veltman DJ (2007 Intrapair differences in hippocampal volume in monozygotic twins discordant for the risk for anxiety and depression. Biol Psychiatry 61:1062–1071

Deckersbach T, Otto MW, Savage CR, Baer L, Jenike MA (2000) The relationship between semantic organization and memory in obsessive-compulsive disorder. Psychother Psychosom 69:101–107

Delorme R, Golmard JL, Chabane N, Millet B, Krebs MO, Mouren-Simeoni MC, Leboyer M (2005) Admixture analysis of age at onset in obsessive-compulsive disorder. Psychol Med 35: 237–243

Denys D, de Geus F, van Megen HJ, Westenberg HG (2004) Symptom dimensions in obsessive-compulsive disorder: factor analysis on a clinician-rated scale and a self-report measure. Psychopathology 37:181–189

Derisley J, Libby S, Clark S, Reynolds S (2005) Mental health, coping and family-functioning in parents of young people with obsessive-compulsive disorder and with anxiety disorders. Br J Clin Psychol 44:439–444

do Rosario-Campos MC, Leckman JF, Curi M, Quatrano S, Katsovitch L, Miguel EC, Pauls DL (2005) A family study of early-onset obsessive-compulsive disorder. Am J Med Genet B Neuropsychiatr Genet 136:92–97

Eysenck J, Eysenck S (1964) Eysenck personality inventory. Educational Industrial Testing Service, San Diego

Fraga MF, Ballestar E, Paz MF, Ropero S, Setien F, Ballestar ML, Heine-Suner D, Cigudosa JC, Urioste M, Benitez J, Boix-Chornet M, Sanchez-Aguilera A, Ling C, Carlsson E, Poulsen P, Vaag A, Stephan Z, Spector TD, Wu YZ, Plass C, Esteller M (2005) Epigenetic differences arise during the lifetime of monozygotic twins. Proc Natl Acad Sci USA 102:10604–10609

Geller D, Doyle R, Shaw D, Mullin B, Coffey BJ, Petty C, Vivas F, Biederman J (2006) A quick and reliable screening measure for OCD in youth: reliability and validity of the obsessive compulsive scale of the child behavior checklist. Compr Psychiatry 47:234–240

Helbing J (1982) Dutch version of the Rosenberg self-esteem scale, a widely used, reliable and valid measure. Ned Tijdschr Psychol 37:257–277

Hudziak JJ, van Beijsterveldt CE, Althoff RR, Stanger C, Rettew DC, Nelson EC, Todd RD, Bartels M, Boomsma DI (2004) Genetic and environmental contributions to the child behavior checklist obsessive-compulsive scale: a cross-cultural twin study. Arch Gen Psychiatry 61:608–616

Huizink AC, Mulder EJ, Buitelaar JK (2004) Prenatal stress and risk for psychopathology: specific effects or induction of general susceptibility? Psychol Bull 130:115–142

Jonnal AH, Gardner CO, Prescott CA, Kendler KS (2000) Obsessive and compulsive symptoms in a general population sample of female twins. Am J Med Genet 96:791–796

Kendler KS, Gardner CO, Prescott CA (1999) Clarifying the relationship between religiosity and psychiatric illness: the impact of covariates and the specificity of buffering effects. Twin Res 2:137–144

Lehn H, Derks EM, Hudziak JJ, Heutink P, van Beysterveldt TCEM, Boomsma DI (2007) Attention problems and attention deficit hyperactivity disorder in discordant and concordant MZ twins: evidence of environmental mediators. J Am Acad Child Adolesc Psychiatry 46:83–91

Lewis CA, Joseph S (1995) Convergent validity of the depression–happiness scale with measures of happiness and satisfaction with life. Psychol Rep 76:876–878

Lochner C, du Toit PL, Zungu-Dirwayi N, Marais A, van Kradenburg J, Seedat S, Niehaus DJ, Stein DJ (2002) Childhood trauma in obsessive-compulsive disorder, trichotillomania, and controls. Depress Anxiety 15:66–68

Lochner C, Hemmings SM, Kinnear CJ, Moolman-Smook JC, Corfield VA, Knowles JA, Niehaus DJ, Stein DJ (2004) Gender in obsessive-compulsive disorder: clinical and genetic findings. Eur Neuropsychopharmacol 14:105–113

March JS, Johnston H, Greist JH (1990) Frontiers of research in obsessive-compulsive disorder. In: Jenike MA, Baer L, Minichiello WL (eds) Obsessive—compulsive disorders—theory and management, 2nd edn. Year Book Medical Publishers Inc, Chicago, pp 349–363

Martin N, Boomsma D, Machin G (1997) A twin-pronged attack on complex traits. Nat Genet 17:387–392

McFall RM, Treat TA (1999) Quantifying the information value of clinical assessments with signal detection theory. Annu Rev Psychol 50:215–241

Meyer U, Schwendener S, Feldon J, Yee BK (2006) Prenatal and postnatal maternal contributions in the infection model of schizophrenia. Exp Brain Res 173:243–257

Nelson EC, Hanna GL, Hudziak JJ, Botteron KN, Heath AC, Todd RD (2001) An obsessive-compulsive scale of the child behavior checklist: sensitivity, specificity, and predictive power. Pediatrics 108:1–5

Nestadt G, Bienvenu OJ, Cai G, Samuels J, Eaton WW (1998) Incidence of obsessive-compulsive disorder in adults. J Nerv Ment Dis 186:401–406

Nestadt G, Samuels J, Riddle MA, Bienvenu OJ III, Liang KY, LaBuda MC, Walkup JT, Grados M, Hoehn Saric R (2000) A family study of obsessive-compulsive disorder. Arch Gen Psychiatry 57:358–363

Nigg JT, Breslau N (2007) Prenatal smoking exposure, low birth weight, and disruptive behavior disorders. J Am Acad Child Adolesc Psychiatry 46:362–369

Olatunji BO, Abramowitz JS, Williams NL, Connolly KM, Lohr JM (2006) Scrupulosity and obsessive-compulsive symptoms: confirmatory factor analysis and validity of the Penn Inventory of Scrupulosity. J Anxiety Disord. E-pub ahead of print

Pauls DL, Alsobrook JP, Goodman W, Rasmussen S, Leckman JF (1995) A family study of obsessive-compulsive disorder. Am J Psychiatry 152:76–84

Perneger TV (1998) What's wrong with Bonferroni adjustments. BMJ 316:1236–1238

Rosenberg M (1965) Society and the adolescent self-image. Princeton University Press, Princeton

Sanavio E (1988) Obsessions and compulsions: the Padua Inventory. Behav Res Ther 26:169–177

Skoog G, Skoog I (1999) A 40-year follow-up of patients with obsessive-compulsive disorder. Arch Gen Psychiatry 56:121–127

Sorensen CB, Kirkeby L, Thomsen PH (2004) Quality of life with OCD. A self-reported survey among members of the Danish OCD association. Nord J Psychiatry 58:231–236

Spielberger CD, Gorsuch RL, Lushene RE (1970) STAI manual for the State Trait Anxiety Inventory. Consulting Psychologists Press, Palo Alto

Stabenau JR, Pollin W (1993) Heredity and environment in schizophrenia, revisited. The contribution of twin and high-risk studies. J Nerv Ment Dis 181:290–297

Stewart SE, Geller DA, Jenike M, Pauls D, Shaw D, Mullin B, Faraone SV (2004) Long-term outcome of pediatric obsessive-compulsive disorder: a meta-analysis and qualitative review of the literature. Acta Psychiatr Scand 110:4–13

Stewart SE, Yen CH, Stack DE, Jenike MA (2006) Outcome predictors for severe obsessive-compulsive patients in intensive residential treatment. J Psychiatr Res 40:511–519

Swets JA (1996) Signal detection theory and ROC analysis in psychological diagnostics: collected papers. Erlbaum, Mahwah

Tek C, Ulug B (2001) Religiosity and religious obsessions in obsessive-compulsive disorder. Psychiatry Res 104:99–108

Van den Hove DL, Steinbusch HW, Scheepens A, van der Berg WD, Kooiman LA, Boosten BJ, Prickaerts J, Blanco CE (2006) Prenatal stress and neonatal rat brain development. Neuroscience 137:145–155

van der Ploeg H, Defares PB, Spielberger CD (1979) Zelfbeoordelingsvragenlijst STAI versie DY-1 en DY-2. Swets and Zeitlinger BV, Lisse

van der Velden PG, van der Burg S, Steinmetz CHD, van den Bout J (1992) Slachtoffers van bankovervallen [Victims of bank robberies]. Bohn Stafleu Van Loghum, Houten

van Grootheest DS, Bartels M, Cath DC, Beekman AT, Hudziak JJ, Boomsma DI (2007a) Genetic and environmental contributions underlying stability in childhood obsessive-compulsive behavior. Biol Psychiatry 61:308–315

van Grootheest DS, Cath DC, Beekman AT, Boomsma DI (2007b) Genetic and environmental influences on OC symptoms in adults: a population based twin-family study. Psychol Med (in press). doi:10.1017/S0033291707000980

van Oppen P (1992) Obsessions and compulsions: dimensional structure, reliability, convergent and divergent validity of the Padua Inventory. Behav Res Ther 30:631–637

van Oppen P, Hoekstra RJ, Emmelkamp PMG (1995) The structure of obsessive-compulsive symptoms. Behav Res Ther 33:15–23

Vasconcelos MS, Sampaio AS, Hounie AG, Akkerman F, Curi M, Lopes AC, Miguel EC (2007) Prenatal, perinatal, and postnatal risk factors in obsessive-compulsive disorder. Biol Psychiatry 61:301–307

Verhulst FC, van der Ende J, Koot HM (1997) Handleiding voor de youth self report. Afdeling Kinder—en Jeugdpsychiatrie, Sophia Kinderziekenhuis/Erasmus Universiteit Rotterdam, Rotterdam

Wichers MC, Purcell S, Danckaerts M, Derom C, Derom R, Vlietinck R, van Os J (2002) Prenatal life and post-natal psychopathology: evidence for negative gene-birth weight interaction. Psychol Med 32:1165–1174

Wilde GJS (1970) Neurotische labiliteit gemeten volgens de vragenlijstmethode [The questionnaire method as a means of measuring neurotic instability]. van Rossum Uitgeverij, Amsterdam

Willemsen G, Posthuma D, Boomsma DI (2005) Environmental factors determine where the Dutch live: results from the Netherlands twin register. Twin Res Hum Genet 8:312–317

Wolf SS, Jones DW, Knable MB, Gorey JG, Lee KS, Hyde TM, Coppola R, Weinberger DR (1996) Prediction of phenotypic variation in monozygotic twins by caudate nucleus D2 receptor binding. Science 273:1225–1227