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Abstract

In this qualitative systematic review, we evaluate studies of the demographic, innate, and environmental risk factors and correlates associated with the development of Obsessive-Compulsive Disorder (OCD) in epidemiological samples. We found that a significant proportion of the studies indicate that late adolescence is a period of increased vulnerability for the development of OCD; that OCD affects predominantly female adults and male children and adolescents; that those who are unmarried or abusing drugs are more likely to present with OCD; that OCD is a familial and genetic disorder, particularly when one considers symptom dimensions instead of categorical diagnosis and when the disorder begins at an early age; and that individuals with OCD from the community, like those seen in clinical settings, may be especially prone to present psychiatric conditions such as mood and anxiety disorders. Although there are plenty of data on the correlates and risk factors of OCD in epidemiological samples, more research is needed on other potential risk factors, including obstetrical and pregnancy problems, pre-morbid neurocognitive functioning, and streptococcal infections, among others.
THE ANALYTICAL EPIDEMIOLOGY OF OBSESSIVE-COMPULSIVE DISORDER

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RUNNING HEAD: The analytical epidemiology of OCD

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ABSTRACT

In this qualitative systematic review, we evaluate studies of the demographic, innate, and environmental factors associated with the development of Obsessive-Compulsive Disorder (OCD) in epidemiological samples. We found that a significant proportion of the studies indicate that late adolescence is a period of increased vulnerability for the development of OCD; that OCD affects predominantly female adults and male children and adolescents; that those who are unemployed, unmarried, non-white, living in urban areas, or abusing drugs are at increased risk for OCD; that OCD in some cases is a familial, and perhaps genetic disorder, particularly when considering symptom dimensions instead of categorical diagnosis, and when the disorder begins at an early age; that individuals with OCD from the community may be especially prone to present low IQ scores and psychiatric conditions such as mood and anxiety disorders; and that, despite a number of studies indicating that streptococcal infection may trigger OCD in clinical samples, there are almost no studies on this issue using community-based samples. Although there are plenty of data on the correlates of OCD in epidemiological samples, more research is needed on its risk factors.
INTRODUCTION

Obsessive-compulsive disorder (OCD) is characterized by the presence of recurrent, persistent and unwanted thoughts, impulses, or images that the person attempts to ignore, suppress or to neutralize with some other thought or action (i.e. obsessions), and by repetitive behaviors (e.g., hand washing, ordering, or checking) or mental acts (e.g., praying, counting, or repeating words silently) that the person feels driven to perform in response to an obsession or according to rules that must be applied rigidly (i.e. compulsions). To meet current diagnostic criteria for OCD, a patient must display either obsessions or compulsions that result in marked anxiety or distress, are time consuming (take more than 1 hour a day), or significantly interfere with the person's normal routine, occupational (or academic) functioning, or usual social activities or relationships (APA, 2000).

According to studies that employed the Composite International Diagnostic Instrument (CIDI) to diagnose OCD, the one-month prevalence of OCD ranges from 0.3 to 3.1% of the general population (Fontenelle et al., 2006), while its one-year incidence is closer to 0.2% (De Graaf et al., 2002). It has been argued that such heterogeneity may stem from factors such as the technical skills of the interviewers (mental health professionals vs. lay personnel), the setting of the evaluation (interviews conducted personally vs. interviews by telephone), the use of technological aids such as computer-assisted assessments, and the intrinsic characteristics of the population under study. Apart from epidemiological inconsistencies, it is clear that a significant number of individuals in the community
suffer from OCD. Therefore, the identification of risk factors for the development of this disorder is critical in the development of prevention and treatment programs.

Although the terms *risk factors* and *correlates* are used rather freely and interchangeably in the epidemiological literature of OCD, appropriate terminologies need to be considered to ensure that scientists communicate more accurately and consistently with clinicians, policymakers, and the broader public, so that their research data are not misunderstood or misapplied (Kraemer et al., 1997). According to Kraemer et al. (1997), if a given factor precedes the outcome in question, this justifies use of the term *risk factor*. If precedence cannot be demonstrated, either *concomitants* or *correlates* are appropriate terms.

In this qualitative systematic review, our objective is to describe the findings regarding the analytical epidemiology of OCD, i.e. the epidemiological data about the risk factors and correlates of OCD. More specifically, we aim to describe the demographic characteristics (especially age, gender, marital status, and social class), innate features (such as season of birth, pregnancy, birth complications, and familial background), environmental factors associated with the development of OCD in community samples and psychiatric comorbidity.

**METHODS**

We searched for articles on the PubMed electronic bibliographic database using the following combination of medical subject heading (MeSH) terms: obsessive-compulsive disorder [MeSH terms] AND (epidemiology[MeSH Terms]
OR epidemiologic factors [MeSH Terms] OR prevalence [MeSH Terms] OR incidence [MeSH Terms]). We restricted our search strategy by means of the limits function available on the PubMed: only studies in English, German, French, Portuguese, or Spanish were selected. Additional studies were selected by using alternative search strategies. The reference lists of the articles identified through these methods were further explored. Book chapters on the epidemiology of OCD, their references, as well as scientific symposia records, were also assessed.

Only cross-sectional or follow-up studies of non-clinical samples describing correlates or risk factors for OCD were reviewed in detail. Studies reporting prevalence or incidence rates of OCD but not the variables of interest (i.e. correlates or risk factors) were excluded from our review. Data generated by clinical samples of OCD were only mentioned to put studies with non-treatment seeking individuals in context.

RESULTS

The first author screened a total of 1239 studies available on the Pubmed. A careful analysis of these studies and other manual searches allowed us to select 84 original studies and 16 reviews (either systematic or narrative), all of which were deemed adequate for further assessment. The correlates and risk factors for OCD in epidemiological samples identified in these original investigations were presented into three different categories: demographic characteristics (especially social class, age, gender, and marital status), innate features (season of birth,
pregnancy, birth complications, and familial background), and environmental factors. Accordingly, the results of our review are depicted in the tables 1 (demographic characteristics), 2 (innate features) and 3 (environmental factors).

**DEMOGRAPHIC CORRELATES AND RISK FACTORS**

**Age and age at onset**

It has been reported that current age might be a significant correlate of the development of OCD in most (Thomsen et al., 1993; Valleni-Basile et al., 1996; Heyman et al., 2001; Maggini et al., 2001; Crino et al., 2005) but not all (Guerrero et al., 2003; Mathews et al., 2004) epidemiological samples.

For example, Thomsen et al. (1993) found students in the highest grades to show significantly more obsessive-compulsive symptoms than those of the lowest. Similarly, Valleni-Basile et al. (1996) reported that adolescents who are older are at higher risk for developing OCD. Similarly, in a study with children and adolescents aged 5-15 years, Heyman et al. (2001) divided OCD cases into age bands and found that the rate of OCD increased exponentially as a function of age. In this study, the OCD cases were significantly older than both the normal and the psychiatric controls. Maggini et al. (2001) reported that age was positively correlated with higher scores on the Leyton Obsessional Inventory-Children Version (LOI-CV) among high school students, also suggesting that symptoms in adolescents increase with age. In the study by Crino et al. (2005), older individuals
 (>55 years) were significantly less likely than those in younger age groups to have OCD. Taken together, these findings suggest that older adolescents may be particularly prone to develop OCD.

The issue regarding age at onset in OCD seems to be more complex than that of current age. While the figures for OCD in treatment-seeking samples are heterogeneous (ranging from 15 to 29 years [Fontenelle et al., 2004]), it has been suggested that the age at onset of OCD is relatively higher in the community (Horwath & Weissman, 2000). However, there are some epidemiological studies that report an earlier onset of symptoms. For example, Degonda et al. (1993) and Angst et al. (2004) found that 30% of the individuals from their Swiss sample had developed obsessive-compulsive symptoms by age 15, 50% by the age of 18, and 70% by age 20.

It is possible that these inconsistent findings may reflect the prevailing uncertainty about the ideal way to define age at onset of OCD, i.e. whether it should be considered as the age at which the first subclinical symptoms appeared (Rosário-Campos et al, 2001), the age at which the symptoms became clinically relevant (Fontenelle et al., 2003), or even the age at which a DSM or ICD diagnosis could be established (Fontenelle et al., 2004). Another important issue that should be taken into consideration when analyzing studies about age at onset is the overall poor reliability of studies based on retrospective recall.

Clinical studies have found that adult women develop obsessive-compulsive symptoms earlier than adult men (see Fontenelle et al., 2002), and these findings have been supported by epidemiological studies. Specifically, a study by Nestadt et al. (1998) found that all incident cases among men occurred in subjects who
were between 30 and 44 years of age, whereas the incident cases among women were more frequent in young adults, with a second higher peak in the group of 65 years and older. However no such significant difference was found in other epidemiological samples (Çilli et al., 2004; Mohamaddi et al., 2004).

Some epidemiological studies suggest that aging in adulthood leads to a reduction in the prevalence rates of obsessive-compulsive symptoms (Degonda et al., 1993) and clinically recognized OCD (Fireman et al., (2001). Çilli et al. (2004) argued that this may be particularly true for males: they found that the 1-year prevalence of adult OCD was inversely related to age in males, while it increased with age in females.

**Gender**

Fontenelle et al. (2004) have previously found that clinical samples of adult OCD were, with a few exceptions, almost universally characterized by a relative predominance of females, a feature that is closely mirrored by most epidemiological studies. In fact, 5 of the 28 studies included in the present review reported a predominance of females in epidemiological samples of adult patients with OCD [only Hwu et al., 1989; Faravelli et al., 1989; Almeida-Filho et al., 1997; Bijl et al., 1998; and Andrade et al., 2002, did not]. Although Mathews et al. (2004) reported that male college students had higher total Leyton Obsessional Inventory-Short Version (LOI-SV) scores than female students, they found no significant differences between the proportion of males and females who met cutoff criteria for probable OCD.
In studies of younger populations including children and adolescents, the gender makeup is more diverse. For example, several clinical studies have reported an oversampling of male subjects (Hanna, 1995). Although some have argued that this phenomenon reflects a treatment-seeking bias, our findings suggest that this may not be the case, since several epidemiological studies reported a similar pattern of preponderance (Flament et al., 1988; Zohar et al., 1992; Douglass et al., 1995; Apter et al., 1996, Canals et al., 1997).

However, this issue is far from settled. For example, in studies that employed the Leyton Obsessional Inventory-Children’s Version (LOI-CV) as a screening instrument in samples of children and adolescents, females reported significantly more symptoms and interference than boys in almost all items (Flament et al., 1988; Thomsen et al, 1993; King et al., 1995; Maggini et al., 2001; Brynska and Wolanczyk, 2005). It is conceivable, therefore, that while girls exhibit more obsessive-compulsive symptoms, boys present more full-blown, severe, and/or impairment generating OCD.

**Employment**

Several lines of evidence suggest that unemployment and decreased economic productivity may be associated with OCD in international clinical and epidemiological samples (Karno et al., 1998; Crum and Anthony, 1993; Grabe et al., 2000; Mohammadi et al., 2004; Çilli et al., 2004, Crino et al., 2005; Fontenelle et al., 2004).

Grabe et al. (2000) found significantly higher rates of unemployment in individuals with OCD than in non-affected control subjects. In the study by Crino et
al. (2005), there was a significantly higher prevalence of OCD among those who were unemployed and those who were not in the labor force than among those who were employed. Crum and Anthony et al. (1993) reported that individuals who do not work for pay were older at OCD onset than individuals who did it. Mohammadi et al. (2004) reported that active businessmen displayed lower prevalence rates of OCD in a multivariate model.

It is questionable whether an unfavorable employment status may be a particular characteristic of OCD. For example, although Karno et al. (1988) described a moderate association between OCD and lower job status in their Epidemiological Catchment Area (ECA) based study, the association of mental disorder with unemployment was not found to be specific for OCD.

There are only three studies that have investigated the patient or parent’s occupation of younger OCD patients in epidemiological samples. In the Italian study by Maina et al. (1999), 17-year-olds with OCD did not differ from age-matched subjects without obsessive-compulsive symptoms and other adolescents in terms of job status (student, employed, and unemployed). In a Hawaiian sample, Guerrero et al. (2003) did not find a significant relationship between the presence of OCD in adolescents and the main wage earner’s employment status, a finding that was also reported in Poland by Brynska and Wolanczyk (2005). In sum, no specific relationship between employment and OCD were found in younger samples.
Marital status

Patients being treated for OCD in several countries are less likely to be married than their non-afflicted counterparts (Fontenelle et al., 2004), and similar results have been found some epidemiological samples (Karno et al., 1998; Crum and Anthony, 1993; Grabe et al., 2000; Mohammadi et al., 2004; Çilli et al., 2004, Crino et al., 2005;). In the ECA study, Karno et al. (1988) found that OCD was more prevalent among divorced or separated subjects than among those who were married or single. Nevertheless, for each psychiatric disorder examined, marital status (divorce or separated) was also a significant correlate, suggesting that this status was not specific for OCD. In a Turkish study, Çilli et al. (2004) reported that the divorced, separated, or widowed subjects had approximately 4.2 times the probability of exhibiting OCD.

Other studies were unable to find differences in the marital status of patients with OCD. Although Mohammadi et al. (2004) found that being single decreased the probability of having OCD in Iranians according to univariate models, multivariate models adjusting for gender and residential area demonstrated no significant difference. Similarly, Crino et al. (2005) were unable to find differences for marital status between people with and without OCD in an Australian sample.

Mixed results were obtained in epidemiological studies of individuals with obsessive-compulsive symptoms who did not fulfill the criteria for OCD. While Degonda et al. (1993) did not find differences between Swiss subjects with obsessive-compulsive symptoms and controls, Nestadt et al. (1994) reported that the prevalence of obsessive-compulsive symptoms was even higher among married or widowed north-Americans.
Education

Some clinical studies have suggested higher IQs (Lewis, 1986) and educational achievements characterized individuals with OCD (Fontenelle et al., 2004). However, the literature from community-based epidemiological studies is much more controversial (Degonda et al., 1993; Nestadt et al., 1994; Maina et al., 1999, Guerrero et al., 2003; Mohammadi et al., 2004; Çilli et al., 2004; Crino et al., 2005).

In the study by Degonda et al. (1993), subjects with obsessive-compulsive symptoms differed from controls by exhibiting higher educational levels. Likewise, Mohammadi et al. (2004) found that OCD was significantly more common among individuals with elementary and high school educational levels than among the illiterate. Nestadt et al. (1994) reported similar results: they found that the prevalence of obsessive-compulsive symptoms was higher among those with higher educational attainment.

A small number of studies seem to contradict the association between OCD and higher educational levels. For examples, although Karno et al. (1988) reported that the ECA prevalence of OCD among college graduates was higher than that among those with some college education, the pattern was reversed for high school education, such that the prevalence of OCD among people who had graduated from high school was lower than that of subjects who had completed some high school. Similarly, Guerrero et al. (2003) found that the lower the main wage earners’ education, the higher the rate of OCD among children and
adolescents in Hawaii. Finally, Crino et al. (2005) were unable to find educational differences between people with and without OCD in an Australian sample.

**Race**

The issue of race in OCD remains an understudied topic and was examined in only a few epidemiological studies (Karno et al., 1988; Nestadt et al., 1994; Valleni-Basile et al., 1996; Heyman et al., 2001; Guerrero et al., 2003; Breslau et al., 2006). In the ECA study, Karno et al. (1988) found that black respondents reported significantly less OCD during their lifetime than did non-Hispanic white respondents. This finding led to some speculation about the protective role of the black ethnic identity on the development of OCD. Additional analysis, however, showed that this finding was not specific for OCD. Similarly, in a study by Nestadt et al. (1994), the prevalence of obsessions and compulsions (not necessarily of clinical severity) was higher in whites than in non-whites. Using data from the National Comorbidity Survey Replication (NCS-R), Breslau et al. (2006) were unable to find significant differences in the prevalence of OCD between Hispanic, the non-Hispanic black and non-Hispanic-white.

In sharp contrast with previous suggestions, a study conducted by Valleni-Basile et al. (1996) found that north-American black adolescents were at a higher risk of developing OCD. Similar findings were reported in Britain by Heyman et al. (2001), who described a significantly greater proportion of children from ethnic minorities in the OCD sample compared with the normal or the psychiatric controls. In Hawaii, Guerrero et al. (2003) found that Hawaiians and Samoans were the only ethnic groups with odds ratios greater than 1.0 for being diagnosed with OCD, with
Hawaiians having a 2-fold probability compared to non-Hawaiians. Some data collected from internet-generated samples (Williams et al., 2005), university students (Thomas et al., 2000), and treatment-seeking populations (Fabrega et al., 1988) have also suggested that individuals from ethnic minorities (i.e. Blacks) may endorse some obsessive-compulsive symptoms more frequently (i.e. contamination and washing/cleaning compulsions), a phenomenon that has been ascribed to factors such as different cultural practices and norms regarding normal behaviors (Williams et al., 2005) or positive self-presentation to counter negative stereotypes (Williams et al., 2005).

As can be seen, there is still controversy regarding the role of race as a predisposition factor for the development of OCD, and more studies on this issue seem appropriate.

**Residential area and geographic location**

To the best of our knowledge, only a few studies, with mixed results, attempted to correlate the rates of OCD with the area of residence (urban/rural). Blazer et al. (1985) reported that the prevalence of OCD was similar in rural (2.07%) and urban settings (2.00%). However, significant differences between these areas emerged within certain age groups. Among individuals between the ages of 18 and 24, OCD was significantly more prevalent in urban than in rural households. This pattern was reversed for individuals over 65 years old, for which OCD was significantly more prevalent in rural homes than urban homes. Among African Americans, individuals living in rural setting were more likely to be diagnosed with OCD than those living in an urban setting.
Henderson and Pollard (1988) found that OCD was more prevalent among those living in the city than those living in suburban or rural areas. Likewise, Mohammadi et al. (2004) reported that the frequency of OCD in Iran was higher in urban than in rural areas. On the other hand, Maina et al. (1999) did not find significant differences in the distributions of older adolescents with OCD, those with obsessive-compulsive symptoms, and other adolescent controls by area of residence (central city, inner suburb, or small town/rural) in Turin, Italy.

As previously reported, more consistent findings emerged in cross-national comparisons of prevalence rates of OCD. Horwath and Weissman (2000) reviewed the epidemiology and presentation of OCD according to international studies employing the DIS and found that the lifetime prevalence for OCD is remarkably consistent throughout the cross-national sites. Most of the prevalence rates fell within the range of 1.9 per 100 in Korea to 2.5 per 100 in Puerto Rico. The lifetime prevalence in Taiwan was only 0.7 per 100, and low rates had also been reported for other psychiatric disorders in this country.

Previous studies have suggested that OCD exhibits a certain degree of homogeneity across cultures (Del Porto, 2001). We found that the most common obsessions in the majority of Brazilian samples were by far those involving themes of aggression. Such pattern has not been described in studies from other regions: while religious themes usually prevail in Middle Eastern samples (in two out of three studies), in other countries the issues of contamination and doubt dominate the clinical picture (Fontenelle et al., 2004). In contrast, washing and checking seem to be the predominant compulsions in clinical samples with OCD from across
the world, suggesting that these features are associated with the patient status rather than with OCD itself.

**Socioeconomic status**

Although non-epidemiological studies suggest that individuals with OCD, especially children, may come from families with higher socioeconomic status (Thomsen, 1994), this issue is much more complex from an epidemiological point-of-view, and there is some evidence suggesting that it may reflect some sort of treatment seeking bias (Flament et al., 1988; Degonda et al., 1993; Douglass et al., 1995; Heyman et al., 2001; Valleni-Basile et al., 1996; Angst et al., 2004; Çilli et al., 2004).

Degonda et al. (1993) found that individuals with obsessive-compulsive symptoms were raised in significantly higher social classes than were controls. However, since their study included only five patients with full-blown OCD, no definitive conclusions could be draw with regard to the role of socio-economic issues as significant correlates of the complete syndrome in this sample. Follow-up data on that sample was provided by Angst et al. (2004), who reported no significant difference in the rate of financial problems between individuals with and without obsessive-compulsive symptoms. Vallenı-Basile et al. (1996) found that adolescents from middle to high socio-economic status were at higher risk of developing OCD after 2 years of follow-up. Nevertheless, the odds-ratio was not calculable in this study, as all five cases of incident OCD had medium to high socio-economic status.
In an epidemiological investigation of eating, depressive, and anxiety symptoms in high school students from a semi-rural, middle-class, predominantly white area. Flament et al. (1988) reported that adolescents with OCD or obsessive-compulsive personality disorder did not differ from the general population in terms of socioeconomic status or family constellation. Likewise, in a study by Douglass et al. (1995), the parental education and socioeconomic status of 18-year-olds with OCD were not significantly different from those of healthy subjects and from individuals with other anxiety disorders, major depressive disorder, dysthymia, and conduct disorder. Similarly, in the Turkish study by Çilli et al. (2004), family income did not demonstrate any significant effect on the prevalence rate of OCD.

In a sharp departure from the literature, Heyman et al. (2001) found that 74% of their community child and adolescent subjects with OCD (defined by occupation of head of household) belonged to the lower social classes compared with 47% of the normal controls. These findings suggest that the increased representation of individuals with OCD from the higher socio-economic strata in clinical samples may reflect greater availability of treatment for these individuals.

A brief account of the risk factors and the correlates of OCD and the corresponding strength of the evidence favoring them are depicted in table 1.

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INNATE CORRELATES AND RISK FACTORS

Familial background and history

The results from twin and family studies suggest that transmission and expression of OCD and milder OCD-related phenotypes are genetically mediated. Further, it was already suggested that there might be an “OCD spectrum” of disorders that share some of the same vulnerability genes, such as Tourette disorder, body dysmorphic disorder, grooming behaviors and obsessive-compulsive personality disorder (Miguel et al., 2005). Even though the genetic transmission of OCD is indisputable, the mode of transmission and the genes involved are still unknown.

Several methodologically rigorous family studies of OCD were conducted during the last 30 years (McKeon and Murray, 1987; Black et al. 1992; Pauls et al. 1995; Nestadt et al. 2000; Nestadt et al., 2001; Reddy et al., 2001; Carter et al., 2004; Rosário-Campos et al., 2005; Fyer et al., 2005; Lipsitz et al., 2005; Hanna et al., 2005). Most studies (Pauls et al. 1995; Nestadt et al. 2000, Rosário-Campos et al., 2005; Fyer et al., 2005; Hanna et al., 2005) but not all (McKeon and Murray, 1987; Black et al., 1992; Lipsitz et al., 2005) found a familial aggregation of OCD. In fact, the prevalence of the definitive diagnosis of OCD among first degree relatives of patients with OCD ranged from 1 to 11.7%, while that among healthy controls varied from 0 to 2.7% (McKeon and Murray, 1987; Black et al. 1992; Pauls et al. 1995; Nestadt et al. 2000; Fyer et al., 2005; and Lipsitz et al., 2005).

Similar results were obtained in the only family study of individuals with non-treatment seeking OCD: the prevalence of OCD among first-degree relatives of
affected individuals was 10.3% and that among first-degree relatives of controls was 1.2% (Grabe et al., 2006). These finding clearly support and validate the findings on familiality of OCD in treatment samples, and are of special interest because of the absence of selection bias that might occur as a result of treatment seeking behavior for OCD or comorbid disorders that could have triggered treatment seeking (Grabe et al., 2006).

As noted above, all but one study (Fyer et al., 2005) that have investigated the familiality of OCD according to the age of onset in probands found that family history may be particularly related to early-onset (Nestadt et al., 2000; Reddy et al., 2001; Rosário-Campos et al., 2005; Hanna et al., 2005), and possibly tic- and ordering-related OCD (Hanna et al., 2005). Moreover, increased rates of anxiety (Black et al. 1992; Nestadt et al., 2001; Carter et al., 2004; Lipsitz et al., 2005) and affective disorders (Nestadt et al., 2001, Carter et al., 2004), but not of OCD per se, were reported in some studies. However, in another study (McKeon & Murray, 1987) increased rates of psychopathology, but not of OCD or anxiety disorders, were reported among first-degree relatives of probands with OCD.

Cavallini et al. (2000) applied a complex segregation analysis to 141 families of probands affected with eating disorders (89 with anorexia and 52 with bulimia nervosa). Given the hypothesized relationship between OCD, Tourette’s and other tic disorders, we considered these diagnoses as affected phenotype in relatives. In the above-mentioned families, eating disorders and OCD followed a Mendelian dominant model of transmission. When probands were divided according to co-diagnosis of OCD, a Mendelian dominant model of transmission best fit the subgroup of families of 114 probands without OCD co-diagnosis, whereas a
Mendelian *additive model of transmission* represented best fit in the subgroup of families of 27 probands with an OCD co-diagnosis.

Twin and adoption studies may help to shed light on the roles played by genes and environment in the etiology of OCD. While adoption studies are generally rare and are not available in the OCD literature, at least 28 twin studies of patients with obsessive-compulsive symptoms have been published with different methodologies and mixed results (as reviewed by Grootheest et al., 2005). Twin studies are based on the assumption that monozygotic (MZ) twins are genetically identical and that dizygotic (DZ) twins share 50% of their genes. If MZ twins resemble each other more than DZ twins, this is indicative of the importance of genetic influences on the trait under consideration. Twin studies employing dimensional approaches may be more desirable, particularly considering that OC symptoms may be more heritable than DSM-IV or ICD-10 OCD, since the impairment criterion may lead to a relative increase in the impact of environmental factors.

According to Grootheest et al. (2005), twin studies of OCD are generally one of the following types: (1) older case-studies of twins with non-standardized diagnosis of OCD; (2) twin studies with the diagnosis of OCD based on operationalized, categorical criteria; (3) twin studies with the diagnosis of OCD using a dimensional approach; and (4) twin studies using both OCD diagnostic criteria and OC symptom dimensions, analyzing the data with Structural Equation Modeling. Grootheest et al. (2005) argued that only the studies using the last method have convincingly shown that obsessive-compulsive symptoms are heritable, with genetic influences in the range of 45% to 65% in children and 27%
to 47% in adults. Nevertheless, a large twin study using a biometrical approach with continuous data is still needed to provide conclusive evidence.

Hasler et al (2006) identified OCD symptom dimensions by performing a factor analysis on a range of OCD symptom categories in a well-defined sample of 418 affected sibling pairs with OCD. The authors analyzed correlations between siblings on the YBOCS symptom categories and the symptom dimensions derived from factor analysis, and evaluated the relationship of psychiatric comorbidity to these dimensions. They found robust sibling–sibling intraclass correlations for two of the four YBOCS factors: the hoarding obsessions and compulsions factor and the aggressive, sexual, and religious obsessions, and checking compulsions factor. A smaller, but still significant, familiality was found for the contamination/cleaning factor and the symmetry, ordering, and arranging factor. This suggests that OC symptom dimensions are influenced by familial, and perhaps genetic, factors. The familiality of factor-analyzed OCD symptom dimensions seemed to be gender-dependent, with higher familiality estimates in women than in men.

To our knowledge, only four community-based inquiries have investigated the family history of patients with obsessive-compulsive symptoms or OCD. Unfortunately, no consistent pattern of family background has emerged (Degonda et al., 1993; Nestadt et al., 1994; Roussos et al., 2003; Grabe et al., 2006).

Degonda et al. (1993) reported that the first-degree relatives of subjects with OC symptoms did not differ from those of controls with respect to obsessive-compulsive, depressive, and anxiety symptoms reported by the probands. In contrast, in an interesting study conducted by Roussos et al (2003), a positive family history of OCD, obsessive-compulsive disorder personality disorder, or
obsessive-compulsive symptoms increased the risk of children with high Leyton Obsessional Inventory-Child Version scores to develop full-blown OCD in a 2-year follow-up. Nestadt et al. (1994) found that subjects with obsessions and compulsions were more likely to report a history of alcoholism and suicidal behavior in first- and second-degree relatives. They also were more likely to characterize the personality of their biological fathers as maladjusted.

**D8/17**

According to controlled clinical studies conducted in the 1990s, a B-lymphocyte marker (D8/17) was found to be over-expressed in patients with Sydenham’s chorea and pediatric autoimmune neuropsychiatric disorder associated with group A streptococcal infection (a condition that included OCD and tic disorders, also known by the acronym PANDAS), suggesting that this marker may predispose individuals to poststreptococcal disease of the central nervous system (Swedo et al., 1997; Dale, 2005).

Based on this association, Inoff-Germain et al. (2003) investigated the role of D8/17 marker as a risk factor for OCD, tics, and other neuropsychiatric disorders in a community sample from a low socio-economic area of Mexico City. Unexpectedly, they found that the reported rates of OCD, tics and other disorders were not higher in the individuals from the group positive for the D8/17. Although these findings have somewhat weakened the D8/17 hypothesis, Inoff-Germain speculated that the absence of association between OCD, tics and other neuropsychiatric disorders and D8/17 may be ascribed to the lack of exposure to
the specific strains of the group A beta-hemolytic streptococcal infections during the study period and the decline in the incidence of rheumatic fever in Mexico City.

**Intelligence levels**

Before the widespread use of psychometric measures to assess intellectual functioning, psychiatrists had assumed that patients with OCD were of superior intelligence (Lewis, 1936), an assumption that was supported by earlier studies (Eysenck, 1947; Ingram, 1961). However, more recent evaluations with clinical populations have cast doubt on the “superior intelligence” claim (Fontenelle et al., 2005), and some (Zohar et al., 1992; Heyman et al., 2001) but not all (Douglass et al., 1995) findings from epidemiological studies suggest that children with OCD are actually less intelligent than the average ones. Zohar et al. (1992) found that their group of adolescents with OCD was significantly lower on intelligence (based on combined score from a version of the Raven Progressive Matrices and an Otis-type verbal test) than the group without OCD. In the study by Heyman et al. (2001), the mean British Picture Vocabulary Scale (BPVS-11) IQ of the 25 cases of children and adolescents with OCD was 87.4. On the other hand, the mean BPVS-11 IQ in the emotional disorders control group was 95.7 and in the normal controls group was 101.8, both scores significantly higher than those of the individuals with OCD. Low IQ could not be accounted for by comorbid conduct disorder or low socio-economic status.

In the study by Douglass et al. (1995), three WISC-R IQ scores obtained at ages 7, 9 and 11 were summed to create a cumulative index of IQ. Although the OCD group had the highest mean IQ score, this finding was not significantly
different from the psychologically healthy control group, the conduct disorder group, or the mixed anxiety/depressive disorder group. The maternal IQ (based on the SRA Verbal test) did not differ among the groups, and the individuals with OCD did not perform significantly differently than the other groups on any of the seven neuropsychological tests, which were administered at age 13.

While it seems unlikely that the early clinical observations and psychometric assessments of patients with OCD were either mistaken or inaccurate (Tallis, 1995), perhaps these inconsistencies from clinical and epidemiological studies can be explained with respect to the heterogeneity of OCD. It had been suggested that OCD is a multifaceted disorder, with several different subtypes and patterns of cognitive dysfunction (Fontenelle et al., 2005). Another important factor that may explain those inconsistencies is the impairment criterion of OCD, as low IQ is certainly related to impaired functioning.

A brief account of the risk factors and the correlates of OCD and the corresponding strength of the evidence favoring them are depicted in table 2.

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ENVIRONMENTAL CORRELATES AND RISK FACTORS

Season of birth and other time trends

According to our review, only two studies have addressed the issue of seasonality of birth in patients with OCD (Greenberg, 1980; Atladottir et al., 2007).
Patients with obsessive-compulsive neurosis who were admitted for the first time to hospitals in England and Wales during 1970-1978 were compared with a 1% sample of the 1971 census for monthly and quarterly distribution of the births of the separate sexes (Greenberg, 1980). The distribution of the month of birth of patients closely resembled that of the general population. Despite these early negative results, we feel that the issue of seasonality of birth in OCD remains unclear, since no study employing modern criteria has been conducted.

Atladóttir et al. (2007) examined the seasonal variations of birth of children diagnosed with autism, hyperkinetic disorder (HD), Tourette syndrome, and OCD. In their study, 669,995 Danish children born from 1990 through 1999 were assessed from 1995 to 2001 using the Danish National Psychiatric Registry, a databank based on the International Classification of Diseases, 10th edition, diagnostic coding system. Similarly to Greenberg (1980), they were unable to find variations in season of birth for OCD or any other of the 3 disorders.

Since several studies report consistent increases in the prevalence of autism in recent years, Atladóttir et al. (2007) investigated whether such time trends were specific for autism or comparable to that of other childhood neuropsychiatric disorders, i.e. HD, Tourette syndrome, and OCD. Using the same database described above, Atladóttir et al. (2007) found that each successive birth cohort had a significantly higher cumulative incidence of Autism, HD, and Tourette syndrome than the previous cohort. No significant change in cumulative incidence was observed for OCD. Therefore, it seems that, differently from other childhood neuropsychiatric disorders, the incidence of OCD during the last years has remained relatively stable.
**Birth Order and Family Size**

Kayton and Borge (1967) suggested that OCD is disproportionately represented in individuals who were either firstborn or only children. They reasoned that these children might be more vulnerable due to precocious ego-development, parental expectations of higher achievement, and pressure to assume more responsibility due to relative parental inexperience.

Some earlier studies on birth order and OCD supported these initial findings (Snowdon, 1979; Coryell, 1981). Nevertheless, different findings were reported in more recent inquiries, which employed modern criteria (DSM-III; Khanna and Channabasavanna, 1987; Pollard et al., 1990). Likewise, with the exception of Okasha (2001), most epidemiological studies did not find increased rates of first-born children among patients with OCD (Nestadt et al., 1994; Nestadt et al., 1998; Heyman et al., 2001; Çilli et al., 2004; Brynska and Wolanczyk, 2005). It should also be noted that although Okasha et al. (2001) found that 83.3% of the patients with obsessive-compulsive symptoms were the first children of their families, they did not report the rates in individuals without those symptoms. Curiously, while Kayton and Borge (1967) found a higher proportion of firstborn and only children among males with OCD, Çilli et al. (2004) found that the prevalence rate of OCD among firstborns or only children was significantly higher only in females.

In addition to possible differences in methodology, it was argued that discrepancies between the more recent findings and those of earlier studies were due to (1) a decline over the past 20 years in the percentage of patients with OCD that were firstborn, (2) the inclusion of patients who would be diagnosed by DSM
criteria as having compulsive personality disorder or some other type of anxiety disorder in earlier studies, and (3) an attenuation of more recent societal norms, reflecting more egalitarian attitudes towards boys and girls (Pollard et al., 1990).

Although the initial findings of Kayton and Borge (1967) as well as other studies (Snowden, 1979; Okasha et al., 2001) suggested that patients with OCD may come from smaller families, most recent investigations did not find such a relationship (Pollard et al., 1990, Nestadt et al., 1994, Nestadt et al., 1998; Heyman et al., 2001; Guerrero et al., 2003, Çilli et al., 2004; Brynska and Wolanczyk, 2005).

Curiously, when Çilli et al (2004) compared subjects by number of sibilings (few: one or two; moderate: three to six; many: seven and over), they found a significantly lower prevalence rate among the subjects with a moderate number of sibilings. The significance of these findings, though, is unclear.

In contrast, Heyman et al. (2001) found that children with OCD came from larger families than did normal controls, with a similar trend when those individuals were compared to psychiatric controls. Likewise, in the study by Guerrero et al. (2003), the number of people in the household had a significant positive correlation with OCD, while other measures of socioeconomic status did not. This pattern of correlation was considered consistent with the hypothesis of an infectious cause for OCD.

**Pregnancy and birth complications**

Capstick and Seldrup (1977) cross-matched 33 patients with “obsessional neurosis” for age, sex and source and period of referral with patients from a control group who had never exhibited obsessive-compulsive symptoms (including
individuals with depression, schizophrenia, schizoaffective and manic-depressive states, and anorexia nervosa). The rate of abnormal births (including breech, the use of forceps, and difficult labor, among other) was significantly higher among patients with “obsessional neurosis” than among patients from the control group. Patients with “obsessional neurosis” who had an abnormal birth displayed significantly greater rates of bizarre rituals (“being of a nature outside normal everyday activities”) than patients from the normal birth group.

More recently, in a study with 263 patients with OCD consecutively admitted to treatment, Lensi et al (1996) found that a history of birth trauma (dystocic delivery, involving the application of forceps, a breech presentation or prolonged hypoxia) was reported significantly more often in male than in female patients, who also displayed higher rates of “odd” and superstitious rituals.

In a study of subjects with Tourette syndrome (TS), Santangelo et al (1994) reported that labor complications (especially forceps), maternal smoking, and excessive consumption of caffeine or alcohol by the mother were associated with the development of OCD. Kano et al (2001) found that the rates of TS and OCD were significantly lower in the first-degree relatives of patients with TS whose mothers exhibited major obstetric complications such as forceps delivery, fetal distress, or premature birth, than in those of patients with TS whose mothers had exhibited no such problems. While correction for multiple testing eliminated the significance of these findings, they suggest that environmental events may be relevant for the expression of OCD in some patients.

More recently, Vasconcellos et al. (2006) compared the prenatal, perinatal, and postnatal histories of 68 patients with OCD to those of 70 control subjects
based on the pattern of responses given on a questionnaire focused on aspects of gestation, labor, birth, and early infancy. Patients with OCD and their mothers endorsed several abnormal events with greater frequency than controls, including edema of the hands, feet, or face and excessive weight gain during gestation, *hyperemesis gravidarum*, prolonged labor, preterm birth, and jaundice.

In their study, Vasconcellos et al. (2006) found that prolonged labor and edema during pregnancy remained statistically significant even after socioeconomic status was entered as a covariable in the logistic regression analysis. Since schooling could be another source of bias (assessment bias), Vasconcellos et al. (2006) repeated the same analyses including socioeconomic status and schooling as covariables. In this instance, protracted labor remained as the only significant association, while edema during pregnancy approached significance. It must be stressed, however, that mothers of patients with mental disorders may be more attentive to their own obstetric histories and to the medical histories of their children in an attempt to find an explanation for the disorder.

Despite all of these studies with clinical samples showing a significant link between OCD and pregnancy or birth complications, there is no single community study, to the best of our knowledge, confirming these findings.

According to a recent systematic review (Ross and McLean, 2006), several studies have investigated the extent to which women with OCD report the onset of their illness to be associated with pregnancy or childbirth (Maina et al., 1999; Neziroglu et al., 1992; Williams and Koran, 1997; Buttolph and Holland et al. 1990; Labad et al., 2005). Unfortunately, most of these studies have been retrospective and uncontrolled and therefore subject to remembering or reporting bias.
Nevertheless, these results indicate that as many as 40% of childbearing OCD outpatients have onset during pregnancy and up to 30% have onset during the postpartum period.

In a study reported above, Maina et al. (1999) found that OCD female individuals were more likely than normal female subjects to report exposure to postpartum events in the Paykel's Life Event Schedule. More recently, the same group (Maina et al., 2001) employed the same instrument to evaluate the presence of triggering life-events in 29 women with OCD in comparison with 29 women with bulimia nervosa (BN) matched for age, age at onset, education and marital status, and in 29 control women matched for demographic features. The study demonstrated that the only specific life event that was significantly associated with the onset of OCD was "having a newborn child". No significant differences in frequency and severity of stressful life events were found among the three groups. This research has provided some evidence for the specificity of this association by showing that post partum is not a non-specific risk factor.

Only one community study investigated whether the postpartum period increases the risk of developing OCD. Uguz et al. (2007) assessed 302 women who delivered at a Turkish maternity hospital from August 2005 to November 2005 on the first day and six weeks postnatally. The incidence of OCD was 4% during the postpartum six weeks, a rate that was clearly higher that those reported in most incidence studies (i.e. 0.05 to 0.79; Fontenelle et al., 2006). Although this finding suggests that the postpartum period may be a genuine risk factor for OCD, the absence of a healthy control group followed for six weeks limits this conclusion. In this study, patients with postpartum OCD were characterized by being more
frequently primiparous and displaying higher rates of avoidant and obsessive-compulsive personality disorders than non-postpartum OCD.

**Substance abuse**

Clinical experience suggest that cocaine abuse (Koizumi, 1985; Satel and McDougle, 1991; Weiner et al., 2001) and the continuous use of amphetamines (Borcherding et al., 1990; Serby, 2003) may be associated with stereotypical environment examining, searching and sorting behaviors, and an exacerbation or development of obsessive-compulsive symptoms. In fact, the association between OCD and substance abuse disorders has also been reported in several epidemiological studies of children, adolescents and adults (Crum and Anthony et al., 1993; Kolada et al., 1994; Douglass et al., 1995; Nelson & Rice, 1997; Guerrero et al., 2003).

In their study with data from the ECA, Crum and Anthony (1993) found that the risk for developing OCD among subjects actively using both cocaine and marijuana was up to 7.2 times higher than that of subjects not actively engaged in illicit drug use. Despite this positive association, the authors admitted that a DIS-based diagnosis of OCD might be too over-inclusive by encompassing cocaine-induced repetitive behaviors that may be best understood as a part of the cocaine intoxication.

Likewise, Douglass et al. (1995) reported that, at age 15, individuals with OCD reported using psychoactive substances of abuse (alcohol, cannabis, illegal drugs other than cannabis, or glue) significantly more often than a population-based healthy group and a depressed/anxious group, but not more than a conduct
disorder group. Similarly, Nelson and Rice (1997) suggested that, when alcohol abuse/dependence and OCD coexist in the initial assessment, the temporal stability of the diagnosis of OCD is higher. The link between substance abuse disorders and OCD was further reinforced in the study by Guerrero et al. (2003), who found that illicit substance use (such as marijuana) and the use of alcohol were associated with OCD in an adolescent Hawaiian sample.

There is some evidence suggesting that parental substance abuse during pregnancy may be also a risk factor for OCD. In a large cohort of subjects with Tourette syndrome (N=180), Matthew et al. (2006) found that prenatal maternal smoking was strongly correlated with increased tic severity and with the presence of comorbid OCD. The fact that several different drugs of abuse may function as risk factors for the development of OCD suggest that, by interacting with dopaminergic reward system, in or extra utero, they may trigger OCD in predisposed individuals.

Life events

Although the role of recent life events in precipitating psychiatric disorders has been widely examined, few empirical studies have specifically investigated the occurrence of stressful or potentially triggering events in the history of individuals with OCD. Even fewer studies have investigated life events with reliable and valid instruments or confined themselves to restrictively defined diagnostic groups with matched comparison subjects; e.g. there is no study comparing OCD and major depressive disorder for stressful events (McKeon et al., 1984, Khanna et al., 1988, Maina et al., 1999, Maina et al., 2001; Gothelf et al., 2004).
McKeon et al. (1984) assessed 25 patients with obsessive-compulsive neurosis and matched controls with the Paykel's Life Event Schedule rated for the year prior to the onset of illness and the date of interview, respectively. The mean life event score of patients was significantly higher than that of the control subjects, and this trend spanned the six months prior to the onset of illness. Patients with abnormal personality traits according to the Standard Assessment of Personality Schedule (obsessional, anxious and self-conscious) experienced significantly fewer life events than those without such traits. The authors also noted that serious illness in the subjects and/or in close relatives, arguments, and birth of a child were reported most frequently, although their occurrence was not frequent enough to test for significance.

Khanna et al. (1988) evaluated the life events for a period of one year prior to onset of OCD in 32 subjects with a maximum duration of illness of two years and compared then to a matched healthy volunteer group. They found a significant excess of life events in the six months prior to the onset of the illness. Undesirable, uncontrolled life events in the area of health and bereavement occurred more commonly in OCD than in the control group.

Maina et al. (1999) employed a semistructured interview in accordance with Paykel's Life Event list to evaluate the number and type of stressful life events that occurred in the 12 months before the onset of OCD in 68 patients with OCD and in a group of 68 control subjects. The rates of life events were not significantly different between patients with OCD and healthy subjects, and no differences were detected between male and female OCD patients.
Recently, Gothelf et al. (2004) investigated associations between life events and personality factors in a clinical sample of 28 children and adolescents with OCD, 28 children with several other anxiety disorders, and 24 normal controls using the Life Events Checklist and the Junior Temperament and Character Inventory. In this study, children with OCD had significantly more negative and total life events in the year before the OCD onset. Likewise, no specific event distinguished children with OCD from those with other anxiety disorders, and the only event that was significantly more common in OCD comorbid with another anxiety disorder than in the normal group was a major illness or injury of a relative. Harm avoidance scores correlated positively and significantly with the description of negative life events and their perceived impact.

Only one study assessed an epidemiological sample of subjects with OCD for the presence of general life events (Valleni-Basile et al., 1996). In their two-stage epidemiological study, Valleni-Basile et al. (1996) found that adolescents who had experienced more undesirable and less desirable life-events, according to the Coddington Life Events Scale for Adolescents, were at higher risk for developing OCD.

Although only a limited number of studies have assessed the importance of general life events in patients with OCD, even fewer have evaluated the impact of traumatic (i.e. life-threatening) experiences and their role in the development of OCD in individuals living in the community. Nevertheless, several lines of evidence point toward the existence of an association between the two variables. These provocative findings come from a number of clinical reports of patients who developed OCD after combat exposure, sexual assault, personal violence, and
serious road traffic accidents (Pitman et al., 1993; de Silva and Marks; 1999; Sasson et al., 2005), and from reports of worsening of OCD symptoms after traumatic life events (Tomer et al., 2006). Further, psychopathological (Lipinsky, 1994; Gershuny et al., 2003; Huppert et al., 2005) and neuroimaging studies show important similarities between OCD and post-traumatic stress disorder (PTSD) [Lucey et al., 1991; Rauch et al., 1991].

At least three studies found a significant link between victimization and the development of OCD in the general population (Jordan et al., 1991; Boudreaux et al., 1998; Maes et al., 2000). For example, experiencing a situation during which the person feared serious injury or death was associated with increased risk of developing several psychiatric disorders, including PTSD, major depressive episode, agoraphobia, social anxiety disorder, and OCD (Jordan et al., 1991; Boudreaux et al., 1998; Maes et al., 2000). More strikingly, while PTSD acted as a strong mediator between victimization and most Axis I disorders, rape remained a significant and independent predictor of OCD in one study (Boudreaux et al., 1998).

**Streptococcus infection**

Group A *Streptococcus* can induce autoimmune disease in humans with particular involvement of the heart, joints and brain (Dale, 2005). [autoimmune disease that affects the heart, joints and the brain] Some authors have widened the spectrum of post-streptococcal conditions of the central nervous system (CNS) to include psychiatric conditions such as OCD, movement abnormalities (chorea, tics, dystonia, and Parkinsonism), and sleep dysfunction (Dale, 2005).
The inclusion of OCD and tic disorders in this putative post-streptococcal spectrum was based on several findings, including increased rates of obsessive–compulsive symptoms and full-blown OCD in Sydenham chorea and PANDAS compared with normal controls (Swedo et al., 1989; Asbahr et al., 1996; Swedo et al., 1998; Dale et al., 2004). In one study the incidence of obsessive-compulsive symptoms in patients with rheumatic fever without chorea, although lower than in Sydenham chorea, was higher than in healthy controls, suggesting that brain dysfunction may be occurring even in patients with rheumatic fever without frank chorea (Mercadante et al., 2000).

Several studies have attempted to define the possible role of post-streptococcal autoimmunity in ordinary ‘idiopathic’ tic and obsessive–compulsive disorders, with mixed and sometimes conflicting results (Dale, 2005). Although an outbreak of streptococcal tonsillitis in Rhode Island, USA, during the 1980s was supposedly associated with a ten-fold increase in the incidence of motor tics (without chorea) in that region (Kiessling et al., 1993), epidemiological evidence for an association between OCD and streptococcal infection is currently lacking. Nevertheless, a large study examining the incidence of PANDAS symptoms in normal children seen for sore throat or well-child care in a large pediatric practice found that ill children with group A beta-hemolytic streptococcal infection were not at increased risk for developing PANDAS symptoms compared with children with presumed viral illness or well children (Perrin et al., 2004).
A brief account of the risk factors and/or the correlates of OCD and the corresponding strength of the evidence favoring them are depicted in table 3.

PSYCHIATRIC COMORBIDITY

Although earlier studies were unable to find significant differences between the number and type of comorbid psychiatric disorders found in OCD and those observed in other disorders (Karno et al., 1988), more careful analyses indicated that some particularities associated with OCD. Nestadt et al. (1998) found the lifetime prevalence of other psychiatric disorders to be higher in subjects with incident OCD than in individuals with major depression or phobias. Using the ECA data, Hollander et al. (1996) found that subjects with “complicated” OCD (i.e. OCD with any other DIS-DSM-III psychiatric disorders) were twice as prevalent as were “uncomplicated” OCD subjects (i.e. OCD as the only major lifetime DIS-DSM-III diagnosis), with prevalence rates of 1.4% and 0.7%, respectively.

Hollander et al. (1996) found that subjects with OCD displayed significantly higher rates of childhood conduct symptoms, adult antisocial personality disorder problems, and suicide attempts than did individuals without psychiatric disorders. Subjects with complicated OCD also had higher rates of mild cognitive impairment
on the mini-mental status examination than did subjects with other neuropsychiatric disorders.

Torres et al. (2004) found psychiatric comorbidity to occur in 62% of the subjects with OCD identified in the UK Psychiatric Comorbidity Survey, a rate that was significantly higher than that displayed by individuals with other neuroses (10%). One quarter of subjects with OCD had attempted suicide at some time in their lives, and pure and comorbid cases of OCD did not differ according to most indices of impairment, including suicidal behavior, although pure cases were significantly less likely to have sought help (14% vs. 56%). In the Australian study by Crino et al. (2005), 79.7% of the individuals diagnosed with OCD had another psychiatric disorder. Individuals with OCD were also significantly more likely than people without OCD to have met criteria for at least one affective, anxiety, substance use, or personality disorder. More recently, Hasler et al. (2006)[you may also refer to my Psychiatry Res 2005 paper – I would appreciated it... Hasler, G., LaSalle, V. H., Ronquillo, J., Tunison, S., Cochran, L. W., Greenberg, B. D., Murphy, D. L. (2005) Obsessive-compulsive disorder symptom dimensions show specific relationships to psychiatric comorbidity. Psychiatry Research 135(2): 121-32-you don’t have to change anything else that comes after the references] reported specific relationships between OCD symptom dimensions and psychiatric comorbidity. Factor I (aggressive, sexual, religious and somatic obsessions, and checking compulsions) was positively related to affective disorders and certain anxiety disorders, while Factor II (obsessions of symmetry, and repeating, counting and ordering/arranging compulsions) was positively associated with substance use and eating disorders.
A description of the epidemiological data on OCD according to the most important comorbid psychiatric disorders is given below.

**Schizophrenia-related disorders**

The relationship between OCD and schizophrenia-related disorders has always puzzled psychiatrists. While some investigators have suggested that obsessions may be risk factors or even a preliminary sign of schizophrenia, others have claimed that obsessional thoughts are a neurotic defense against psychotic decompensation. Unfortunately, however, only a few cross-sectional clinical (Poyurovsky et al., 1999; Tibbo et al., 2000; Byerly et al., 2005) and community studies (Karno et al., 1988) have systematically collected data on the temporal relationship between OCD and schizophrenia. Clinical studies have generally agreed that OCD can start first, simultaneously or after schizophrenia (Poyurovsky et al., 1999; Tibbo et al., 2000; Byerly et al., 2005).

Similarly, in the cross-sectional community study by Karno et al. (1988), while schizophrenia more often had an age at onset before that of OCD, comorbid schizophreniform disorder was about equally likely to occur before or later than OCD. The earlier onset of schizophrenia suggests that factors directly (e.g., pathophysiologic changes) or indirectly (e.g., antipsychotic-associated side effects) related to schizophrenia, may be important contributors to the development of OC symptoms in these patients (Byerly et al, 2005). On the other hand, the fact that schizophreniform disorder may occur after OCD is consistent with the view by Insel and Akiskal (1986), according to whom obsessions may evolve into “understandable” secondary delusions or delusion-like ideas [in Jaspers’ terms
if patients with OCD are submitted to significant stressful life events. Clearly, long-term follow-up studies of individuals in community settings are needed to clarify the relationship between OCD and schizophrenia.

Bipolar disorders

In a follow-up study using the North-American ECA data, Crum and Anthony et al. (1993) found that the risk of later OCD was increased for persons with bipolar disorders. Similarly, Grabe et al. (2001) studied the lifetime comorbidity of a sample of 4075 adults living in northern German by means of the CIDI. They found an increased prevalence of bipolar disorders exclusively in female individuals with OCD. In their long-term Swiss follow-up study, Angst et al. (2004) found that the prevalence of OCD or obsessive-compulsive syndromes was significantly increased in the presence of bipolar spectrum disorders, bipolar II disorder, and “minor bipolar disorder”. Angst et al. (2004) argued that their repeated interviews enabled them to identify a far higher number of hidden bipolar cases (around 50% of patients with major depression) and to correct the over-diagnosis of unipolar depression in subjects with OCD.

Major depressive disorder

Several studies found that OCD and major depressive disorder frequently co-occur in epidemiological samples (Crino et al., 2005). Nevertheless, the temporal relationship between these disorders is still a matter for debate. In the study by Karno et al. (1988), respondents who had both lifetime OCD and major depressive disorder frequently reported the onset of OCD before the onset of major
depressive disorder. Likewise, Kessler et al. (2005) analyzed 12-month DSM-IV disorders in the NCS-R and also found OCD to be associated with major depressive episodes. Although they did not analyze specific temporal relationships between the ages at onset of comorbid conditions, they found a later average age at onset for major depressive disorder than for OCD [Kessler et al, 2005].

In contrast, Crum and Anthony et al. (1993) found that the risk of later OCD was increased for persons with baseline major depression. In the above-mentioned study performed in Germany by Grabe et al. (2001), there was an increased prevalence of major depression and dysthymic disorder in individuals with OCD from both genders. Nevertheless, the onset of major depressive disorders occurred to a comparable extent before, in the same year and after the onset of OCD, thus suggesting that depressive disorders may be risk factors, correlates or complications of OCD.

**Anxiety disorders**

In the study by Karno et al. (1988), phobic disorders were earlier occurring disorders than OCD. Accordingly, in the follow-up study using the North-American ECA data, Crum and Anthony et al. (1993) found that the risk of later OCD was increased for persons with phobic disorders. Accordingly, in their Swiss study, Angst et al. (2004) found that the prevalence of OCD or obsessive-compulsive syndromes was significantly increased in the presence of panic disorder, panic attacks, social phobia, and generalized anxiety disorder.

Grabe et al. (2001) observed an increased prevalence of anxiety disorders (specific phobia, generalized anxiety disorder, and post traumatic stress disorder)
exclusively in female individuals with OCD and also that the onset of anxiety disorders occurred before the onset of OCD in most cases. They also found that subjects with OCD with comorbid anxiety disorders had an increased odds ratio for additional depressive disorders and somatoform pain disorder compared to those without any comorbid anxiety disorder.

Brueckl et al. (2007) examined whether separation anxiety disorder (SAD) could be a risk factor for other mental disorders in a 4-year, prospective longitudinal study of a representative cohort of community adolescents and young adults aged 14–24 years at baseline in Munich (n = 1,090). They found that SAD was strongly and independently related not only to OCD, but also to PTSD, bipolar disorder, and alcohol dependence. Brueckl et al. (2007) hypothesized that difficulties in affect modulation may mediate the effects of SAD on various subsequent disorders, including OCD.

**Personality disorders**

At least three studies extend the findings of previous research conducted in clinical populations by demonstrating that personality disorders (PD) are highly prevalent among people with OCD living in the community (Karno et al., 1988; Nestadt et al.1994; Kolada et al., 1994; Torres et al., 2006). Unfortunately, however, these studies were quite heterogeneous in terms of methodology, e.g. the ECA (Karno et al., 1988) and the Edmonton (Kolada et al., 1994) studies ignored the rates of most PD, only reporting the prevalence rates for antisocial personality disorder.
In a more pervasive assessment of PD in a community sample of 810 participants (Nestadt et al., 1994), compulsive, borderline and histrionic PD, but not antisocial, were significantly associated with the presence of obsessions and compulsions. More recently, a secondary analysis of the data from the 2000 British National Survey of Psychiatric Morbidity (Torres et al., 2006) found that approximately 74% of the OCD group met screening criteria for at least one personality disorder, a rate significantly higher than those found in the two other control groups (i.e. 55% of the other neurosis patients and only 24% of the non-neurotic controls). With the exception of histrionic PD, all categories were significantly more prevalent in the OCD group compared to the non-neurotic control group. The rates of paranoid, avoidant, schizotypal, dependent and narcissistic personality disorders were all significantly higher among individuals with OCD than among those with other neuroses. [Is OC personality disorder related or non-related ot OCD? I have heard confusing things about the relationship between OCPS and OCD…]

Other psychiatric disorders

In their study, Grabe et al. (2001) found an increased prevalence of somatoform pain disorder in individuals with OCD from both genders; and of substance dependence (to alcohol, nicotine, and sedative hypnotics), and eating disorders NOS exclusively in female individuals with OCD. In their long-term Swiss follow-up study, Angst et al. (2004) found that the prevalence of OCD or obsessive-compulsive syndromes was significantly increased in the presence of bulimia, binge eating, and marginally with neurasthenia.
Childhood psychiatric disorders

Only a few studies have analyzed the patterns of comorbidities in an epidemiological sample of pediatric OCD (Flament et al., 1988; Zohar et al., 1992; Douglass et al., 1995; Heyman et al., 2001; Guerrero et al., 2003). The first was a high school-based study performed by Flament et al. (1988), who found that 75% of children and adolescents with OCD had one or more lifetime psychiatric diagnoses and 50% had at least one other current diagnosis, including major depression (25%), overanxious disorder (20%), compulsive personality disorder (17%), and bulimia nervosa (17%).

Zohar et al (1992) reported that the rates of Tourette syndrome and transient and chronic motor tics [but not attention deficit hyperactivity disorder (ADHD)] in adolescents identified with OCD were significantly higher than those of age-matched subjects without OCD. Despite these initial negative findings regarding ADHD, Guerrero et al. (2003) reported an association between ADHD and later OCD.

Douglass et al. (1995) found that the prevalence rates of the following disorders were significantly higher in 18-year-old subjects with OCD than in the age-matched control group without OCD: major depressive disorder and dysthymia, social phobia, simple phobia, agoraphobia, alcohol, and marijuana dependence, and conduct disorder. No significant difference was reported in terms of tics. Nevertheless, only depression and substance use in early adolescence were risk factors for OCD in young adulthood. Given the strong link between OCD and depression, Douglass et al. (1995) suggested that future versions of the DSM
might consider the possibility of merging the diagnostic category of OCD with an affective component instead of keeping them as such distinct entities. Finally, although Heyman et al. (2001) found comorbid psychiatric diagnoses in 76% of their sample of children and adolescents with OCD, they did not report the pattern of comorbidities in subjects without OCD, making the interpretation of their findings difficult.

DISCUSSION

There is a great deal of research evidence for correlates of OCD, but less data regarding OCD risk factors (Crum and Anthony et al., 1993; Douglass et al., 1995; Valleni-Basile et al., 1996; Roussos et al., 2003; Inoff-Germain et al., 2003; and Perrin et al., 2004). This deficiency is probably related to the difficulties inherent to the elaboration and implementation of follow-up or incidence studies of OCD, which are fundamental for the evaluation of risk factors (Fontenelle et al., 2006).

Data from follow-up studies suggest that the following individuals from the community may exhibit risk factors for the development of OCD: older (Valleni-Basile et al., 1996) and black adolescents (Valleni-Basile et al., 1996), individuals with fewer desirable or excessive undesirable or traumatic life events (Valleni-Basile et al., 1996; Jordan et al., 1991; Boudreaux et al., 1998; Maes et al., 2000), persons who do not work for pay, especially women (Crum and Anthony et al., 1993), subjects with substance abuse in general (Douglass et al., 1995) or actively using both cocaine and marijuana (Crum and Anthony et al., 1993), individuals with a prior history of alcohol use disorder (Crum and Anthony et al., 1993), persons
exhibiting a syndrome of major depression (including grief reactions) (Crum and Anthony et al., 1993; Douglass et al., 1995), bipolar disorder, and phobic disorder (Crum and Anthony et al., 1993), and those with past history of separation anxiety disorder (Brueckl et al., 2004) or a positive family history for OCD (Roussos et al., 2003).

Since impairment is a criterion for OCD, one should be aware that the data about employment, marital and socioeconomic status, or even intelligence levels as correlates of this disorder might be somewhat circular and not very informative. It would be more instructive to look at associations between the presence and severity of obsessive-compulsive symptoms and impairment. It would also be interesting to compare different psychiatric syndromes (but not impairment-defined disorders) with respect to employment and other social issues to identify specific associations. Major depressive disorder is certainly an important predictor of unemployment, of having no children, and of being unmarried/divorced. Therefore, it would be interesting to see if associated depression also explains social disadvantages among patients with OCD.

If one intends to increase the study on the analytical epidemiology of OCD, some particular methodological difficulties inherent to the study of this disorder should be taken into consideration, particularly those related to biological risk factors. Perhaps the most promising methods to solve these problems would be the adoption of dimensional instead of categorical approaches, the acknowledgement that OCD is a clinically heterogeneous disorder characterized by extremely pleomorphic features, and the understanding that it is associated with an
impressively high comorbidity level. We will discuss these issues in a point-by-point fashion.

Firstly, somewhat inconsistent results generated by twin-studies that employed a categorical approach (e.g. DSM-IV OCD either present or not) are in striking opposition to the positive findings reported by those investigations using obsessive-compulsive symptom dimensions. Since functional impairment is required for the diagnosis DSM-IV OCD and impairment may largely depend on environmental factors (Weissman et al., 2005), this criterion may reflect “noise” in genetic studies in OCD. For example, OC symptoms may increase functionality in some subjects and lead to impairments in others through factors unrelated to OC symptoms (and only the second group be diagnosed with OCD). Therefore, the way of diagnosing OCD may explain some of the discrepancies in the OCD literature.

Secondly, it has been repeatedly demonstrated that OCD is associated with a great heterogeneity of symptoms, a finding that challenges its unitary nosological status. For example, there are still discussions about whether or not hoarding is specific to OCD. The identification of reliable risk factors should take this heterogeneity into consideration.

Thirdly, several studies have found increased rates of comorbid psychiatric disorders (particularly major depressive disorder) among samples with OCD from the general community. For example, as OCD is comorbid with major depression in up to 80-90% of subjects under study (LaSalle et al., 2004), any OCD risk factor may also be a MDD risk factor.
With a very few exceptions (e.g. substance abuse), almost no risk factor described above was replicated in more than one community study. Therefore, there is an urgent need for the development of community-based follow up studies of healthy and at-risk individuals in order to confirm previously suggested risk factors for OCD and to develop measures that can lead to the prevention of this often incapacitating disorder.
<table>
<thead>
<tr>
<th>Demographic features</th>
<th>Positive studies</th>
<th>Negative studies</th>
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</thead>
<tbody>
<tr>
<td><strong>Chronological age</strong></td>
<td>OC symptoms:</td>
<td>OC symptoms:</td>
</tr>
<tr>
<td>Older adolescents ^RF^</td>
<td>Thomsen et al., 1993; Maggini et al., 2001</td>
<td>Mathews et al., 2004</td>
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<tr>
<td></td>
<td>OCD:</td>
<td>OCD:</td>
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<tr>
<td></td>
<td>Valleni-Basile et al., 1996; ^RF^</td>
<td>Guerrero et al., 2003</td>
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<tr>
<td><strong>Age at onset</strong></td>
<td>OC symptoms:</td>
<td>OC symptoms:</td>
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<tr>
<td>Earlier onset in males</td>
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<td></td>
<td>OCD:</td>
<td>OCD:</td>
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<td></td>
<td>Nestadt et al., 1998</td>
<td>Çilli et al., 2004; Mohamaddi et al., 2004</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>OC symptoms:</td>
<td>OC symptoms:</td>
</tr>
<tr>
<td>Female / male ratio &gt; 1 in adults</td>
<td>-----</td>
<td>Mathews et al., 2004</td>
</tr>
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<td></td>
<td>OCD:</td>
<td>OCD:</td>
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<td></td>
<td>Canino et al., 1987; Karno et al., 1988; Henderson et al., 1988; Bland et al., 1988; Wells et al., 1989; Lee et al., 1990; Stefansson et al., 1991; Wittchen et al., 1992; Chen et al., 1993; Nemeth et al., 1997; Jenkins et al., 1997; Almeida-Filho et al., 1997; Wittchen et al., 1998; Grabe et al., 2000; Henderson et al., 2000; Angst et al., 2004; Jacobi et al., 2004; Çilli et al., 2004; Mohamaddi et al., 2004; Faravelli et al., 2004a,b; Crino et al., 2005; Torres et al., 2006;</td>
<td>Hwu et al., 1989; Faravelli et al., 1989</td>
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<tr>
<td>Category</td>
<td>OC symptoms</td>
<td>OC symptoms</td>
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<td>--------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Male / female ratio &gt; 1</td>
<td>OC symptoms: Flament et al., 1988; Thomsen et al, 1993; King et al., 1995;</td>
<td>OC symptoms: Brynska and Wolanczyk, 2005</td>
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<td></td>
<td>Maggini et al., 2001; Brynska and Wolanczyk, 2005</td>
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<tr>
<td></td>
<td>Flament et al., 1988; Thomsen et al, 1993; King et al., 1995; Maggini et al,</td>
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<td></td>
<td>2001; Brynska and Wolanczyk, 2005</td>
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<td></td>
<td>Zohar et al., 1992; Douglass et al., 1995; Takai et al., 1995; Apter et al,</td>
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<td></td>
<td>1996, Canals et al., 1979</td>
<td></td>
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<tr>
<td>Marital status</td>
<td>OC symptoms: Degonda et al., 1993; Nestadt et al., 1994</td>
<td>OC symptoms: Mohammadi et al., 2004; Crino et al., 2005</td>
</tr>
<tr>
<td>Unmarried</td>
<td>OC symptoms: Kano et al., 1998; Crum and Anthony, 1993; Grabe et al., 2000;</td>
<td>OC symptoms: Mohammadi et al., 2004; Crino et al., 2005</td>
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<td></td>
<td>Cinli et al., 2004</td>
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<tr>
<td>Educational levels</td>
<td>OC symptoms: Degonda et al., 1993; Nestadt et al., 1994</td>
<td>OC symptoms: Kano et al., 1988; Crino et al., 2005</td>
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<tr>
<td>Higher</td>
<td>OC symptoms: Kano et al., 1988 (college); Mohammadi et al., 2004;</td>
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<tr>
<td></td>
<td>OC symptoms: Kano et al., 1988; Crino et al., 2005</td>
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<tr>
<td>Race</td>
<td>OC symptoms:</td>
<td>OC symptoms:</td>
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<tr>
<td>Non-whiteRF</td>
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<td>Nestadt et al., 1994</td>
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<td>Residential area</td>
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<tr>
<td><strong>Urban</strong></td>
<td><strong>OCD:</strong> Valleni-Basile et al., 1996; RF Heisman et al., 2001; Guerrero et al., 2003; <strong>OC symptoms:</strong> Maina et al., 1999</td>
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<tr>
<td></td>
<td><strong>OCD:</strong> Karno et al., 1998; Breslau et al., 2006</td>
<td></td>
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<tr>
<td><strong>Non-urban</strong></td>
<td><strong>OCD:</strong> Blazer et al., 1985; Henderson and Pollard, 1988; Mohammadi et al., 1994</td>
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<td></td>
<td><strong>OC symptoms:</strong> Maina et al., 1999</td>
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<tr>
<th>Socioeconomic levels</th>
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<tbody>
<tr>
<td><strong>Higher</strong></td>
<td><strong>OC symptoms:</strong> Degonda et al., 1993</td>
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<tr>
<td></td>
<td><strong>OCD:</strong> Flament et al., 1988; Douglass et al., 1995; Çilli et al., 2004</td>
</tr>
<tr>
<td><strong>Lower</strong></td>
<td><strong>OC symptoms:</strong> Angst et al., 1994; Flament et al., 1988; Douglass et al., 1995;</td>
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<td></td>
<td><strong>OCD:</strong> Heyman et al., 2001</td>
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</tbody>
</table>

Note: RF=Attributes that were shown to be risk factors for OCD in at least one study
Table 2: Innate OCD correlates and risk factors for OCD

<table>
<thead>
<tr>
<th>Innate features</th>
<th>Positive studies</th>
<th>Negative studies</th>
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</thead>
<tbody>
<tr>
<td><strong>Familial factors</strong></td>
<td></td>
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<tr>
<td>First-degree relative with OCD&lt;sup&gt;RF&lt;/sup&gt;</td>
<td>Pauls et al., 1995; Nestadt et al., 2000; Roussos et al., 2003;&lt;sup&gt;RF&lt;/sup&gt; Fyer et al., 2005; Grabe et al., 2006; Reddy et al., 2001 (“Juvenile OCD”); Rosário-Campos et al., 2005 and Hanna et al., 2005 (“Early-onset OCD”);</td>
<td>McKeon and Murray, 1987; Black et al. 1992; Degonda et al., 1993; Lipsitz et al., 2005</td>
</tr>
<tr>
<td>Monozigotic twin with OCD</td>
<td>Inouye et al., 1965; Carey and Gottesman, 1981; Young et al., 1971; Torgersen et al., 1990; Clifford et al., 1984; Jonnal et al., 2000; Eley et al., 2003; Hudziak et al., 2004.</td>
<td>Torgersen et al., 1983; Andrews et al., 1990</td>
</tr>
<tr>
<td><strong>Immunological factors</strong></td>
<td></td>
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<tr>
<td>D8/17</td>
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<td>Inoff-Germain et al., 2003</td>
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<tr>
<td><strong>Neuropsychological factors</strong></td>
<td></td>
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<tr>
<td>Lower IQ</td>
<td>Zohar et al., 1992; Heyman et al., 2001</td>
<td>Douglass et al., 1995</td>
</tr>
</tbody>
</table>

Note: RF=Attributes that were shown to be risk factors for OCD in at least on study; Twin studies are reported in terms of concordance (when a categorical diagnosis is made) or heritability (when dimensional scores are employed). The reader is referred to the text.
Table 3: Environmental OCD correlates in epidemiological studies

<table>
<thead>
<tr>
<th>Environmental features</th>
<th>Positive studies</th>
<th>Negative studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time trends</strong></td>
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<tr>
<td>Seasonality</td>
<td>-----</td>
<td>Greenberg, 1980; Attlaidóttir et al., 2007a</td>
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<tr>
<td>Recent increase in prevalence</td>
<td>-----</td>
<td>Attlaidóttir et al., 2007b</td>
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<tr>
<td>rates</td>
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<tr>
<td><strong>Birth order</strong></td>
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<tr>
<td>First child</td>
<td>Okasha et al., 2001</td>
<td>Nestadt et al., 1994; Nestadt et al., 1998; Heyman et al., 2001; Çilli et al., 2004; Brynska and Wolanczyk, 2005</td>
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<tr>
<td><strong>Family size</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smaller</td>
<td>Okasha et al., 2001</td>
<td>Pollard et al., 1990; Nestadt et al., 1994; Nestadt et al., 1998; Heyman et al., 2001; Guerrero et al., 2003; Çilli et al., 2004; Brynska and Wolanczyk, 2005</td>
</tr>
<tr>
<td>Bigger</td>
<td>Heyman et al., 2001; Guerrero et al., 2003</td>
<td>Pollard et al., 1990; Nestadt et al., 1994; Nestadt et al., 1998; Okasha et al., 2001; Çilli et al., 2004; Brynska and Wolanczyk, 2005</td>
</tr>
<tr>
<td><strong>Pregnancy and delivery</strong></td>
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<tr>
<td>Obstetrical complications</td>
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<tr>
<td>Post-partum period</td>
<td>Uguz et al., 2007</td>
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<tr>
<td><strong>Substance abuse</strong></td>
<td></td>
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<tr>
<td>Cocaine</td>
<td>Crum and Anthony et al., 1993; Nelson &amp; Rice, 1997;</td>
<td>Kolada et al., 1994;</td>
</tr>
</tbody>
</table>
### Alcohol
- Kolada et al., 1994; Douglass et al., 1995; Nelson and Rice, 1997; Guerrero et al., 2003
- Crum and Anthony et al., 1993;

### Marijuana
- Crum and Anthony et al., 1993; Guerrero et al., 2003
- Kolada et al., 1994; Douglass et al., 1995;

### Glue
- Douglass et al., 1995

### Drugs in general
- Guerrero et al., 2003; Douglass et al., 1995; Kolada et al., 1994;

### Parental smoking
- Mathews et al., 2006

#### Life events

**More undesirable life events**
- Valleni-Basile et al., 1996

**Less desirable life events**
- Valleni-Basile et al., 1996

**Traumatic events**
- Jordan et al., 1991; Boudreaux et al., 1998; Maes et al., 2000

#### Infections

**Streptococcal infections**
- -----
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