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Is obsessive-compulsive disorder an anxiety disorder, and what, if any, are spectrum conditions? A family study perspective

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Abstract

Background: Experts have proposed removing obsessive-compulsive disorder (OCD) from the anxiety disorders section and grouping it with putatively related conditions in DSM-5. The current study uses comorbidity and familiality data to inform these issues.

Methods: Case family data from the OCD Collaborative Genetics Study (382 OCD-affected probands and 974 of their first-degree relatives) were compared with control family data from the Johns Hopkins OCD Family Study (73 non-OCD-affected probands and 233 of their first-degree relatives).

Results: Anxiety disorders (especially agoraphobia and generalized anxiety disorder), cluster C personality disorders (especially obsessive-compulsive and avoidant), tic disorders, somatoform disorders (hypochondriasis and body dysmorphic disorder), grooming disorders (especially trichotillomania and pathological skin picking), and mood disorders (especially unipolar depressive disorders) were more common in case than control probands; while the prevalences

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of eating disorders (anorexia and bulimia nervosa), other impulse control disorders (pathological gambling, pyromania, kleptomania), and substance dependence (alcohol or drug) did *not* differ between the groups. The same general pattern was evident in relatives of case versus control probands. Results in relatives did not differ markedly when adjusted for demographic variables and proband diagnosis of the same disorder; though the strength of associations was lower when adjusted for OCD in relatives. Nevertheless, several anxiety, depressive, and putative OCD-related conditions remained significantly more common in case than control relatives when adjusting for all of these variables simultaneously.

Conclusions: On the basis of comorbidity and familiality, OCD appears related both to anxiety disorders and to some conditions currently classified in other sections of DSM-IV.

Introduction

Experts have proposed removing obsessive-compulsive disorder (OCD) from the anxiety disorders section and grouping it with putatively related conditions in DSM-5 (Hollander et al., 2008); this remains controversial (Storch et al., 2008). Proposed OCD-related conditions include obsessive-compulsive personality disorder (OCPD), tic disorders, hypochondriasis, body dysmorphic disorder (BDD), trichotillomania and other grooming disorders, eating disorders, pathological gambling (PG), and other impulse control disorders, including substance dependence (Hollander et al., 2008).

OCD is familial [e.g., (do Rosario-Campos et al., 2005, Fyer et al., 2005, Grabe et al., 2006, Hanna et al., 2005, Nestadt et al., 2000, Pauls et al., 1995)], and this familiality appears mainly due to genetic influences (van Grootheest et al., 2005). Finding that certain conditions are highly comorbid with and familially related to OCD may suggest a genetic relationship between OCD and these other conditions that could inform nosology. The current study examines how commonly anxiety disorders, related personality disorders, and putative “spectrum” conditions occur in OCD-affected probands and their first-degree relatives, compared with control probands/relatives. A higher prevalence of anxiety disorders and related personality disorders in OCD-affected probands and their relatives would support retention of OCD within the anxiety disorders section in DSM-5. A higher prevalence of putative OCD-related conditions in OCD-affected probands and their relatives would support acknowledgement of “OCD spectrum conditions” in DSM-5, whether or not OCD is retained in the anxiety disorders section.

Previous controlled OCD comorbidity and family studies (Bienvenu et al., 2000, Black et al., 1994, Black et al., 1992, Black et al., 1993, Carter et al., 2004, do Rosario-Campos et al., 2005, Fyer et al., 2005, Grados et al., 2001, Jaisoorya et al., 2003, Nestadt et al., 2001, Pauls et al., 1995, Samuels et al., 2000, Torres and Del Porto, 1995) are summarized in Table 1. Results of these studies suggest that some anxiety disorders (esp. generalized anxiety disorder or GAD) are relatively common in persons with OCD and their first-degree relatives. Cluster C (“anxious cluster”) personality disorders (Bienvenu and Stein, 2003), esp. OCPD, also appear relatively common in persons with OCD and, perhaps, their first-degree relatives. In addition, tic disorders, hypochondriasis, BDD, and “grooming” disorders (pathological nail biting or PNB, pathological skin picking or PSP, and trichotillomania),

appear relatively common in persons with OCD and, perhaps, their first-degree relatives. Conversely, PG, kleptomania, pyromania, alcohol dependence, and drug dependence do not appear particularly common in persons with OCD or their family members. Based on these previous results, we predicted that at least some anxiety disorders and OCPD would be highly comorbid in OCD-affected probands and would segregate in their families. We also predicted that tic disorders, hypochondriasis, BDD, and "grooming" disorders would be highly comorbid in OCD-affected probands and would segregate in their families, but not PG, other impulse control disorders, or substance use disorders.

Method

Sample

This project uses control family data from the Johns Hopkins OCD Family Study [JHOFS (Nestadt et al., 2000)], and case family data from the OCD Collaborative Genetics Study [OCGS (Samuels et al., 2006)]. In the JHOFS, we directly interviewed 73 community control probands and 233 of their first-degree relatives, blind to proband/family status, between 1995 and 1999. The control probands were selected to demographically match case probands from OCD specialty treatment centers in the Baltimore, MD, and Washington, DC, area (Nestadt et al., 2000). [Note that, since we have reported on JHOFS *case* probands and relatives previously (Bienvenu et al., 2000, Grados et al., 2001, Nestadt et al., 2001, Samuels et al., 2000), these participants are excluded in the current study. Also, we only include JHOFS data from participants who were *directly* interviewed in the current study, for the sake of comparability of methods across studies.]

In the OCGS, collaborators at Brown University (Butler Hospital), Columbia University, Massachusetts General Hospital, Johns Hopkins University (JHU), the National Institute of Mental Health, and the University of California in Los Angeles interviewed over 400 families between 2001 and 2008; JHU was the coordinating center for the study (Samuels et al., 2006). Participants were recruited from outpatient and inpatient clinics, referrals from clinicians in the community, web sites, media advertisements, self-help groups, and Obsessive-Compulsive Foundation annual conventions. The OCGS targeted families with OCD-affected sibling pairs and extended these when possible through affected relatives; in addition, two sites (JHU and Columbia) collected additional pedigrees with multiple affected relatives when available. [Note that we only include OCGS data from probands and *first*-degree relatives in the current study, for the sake of comparability of data across studies. In addition, though the OCGS included probands younger than age 18 years, we excluded these families in the current study, again for the sake of comparability of data across studies. The resulting data set included 382 case probands and 974 of their first-degree relatives.]

In both the JHOFS and the OCGS, probands were excluded if they had schizophrenia, mental retardation, dementia, or Tourette's disorder. In addition, control probands were excluded if they had OCD (JHOFS), while case probands were included if they had OCD – but not if OCD occurred only during a major depressive episode. In the OCGS, proband OCD symptoms had onset before age 18 years. In both the JHOFS and the OCGS, after a complete description of the study to the participants, written informed consent (or assent, for children) was obtained.

Diagnostic procedures

Doctoral-level clinicians made lifetime DSM-IV diagnoses using modified semi-structured interviews: the Schedule for Affective Disorders and Schizophrenia – lifetime anxiety version (SADS-LA – Mannuzzaet al., 1986) and Kiddie-SADS (Kaufman et al., 1997) (JHOFS), the Structured Clinical Interview for DSM-IV (First et al., 1996) (OCGS), and the Revised Structured Instrument for the Diagnosis of Personality Disorders (Pfohl et al., 1989). The OCD section was adapted from the SADS-LA to include detailed screening questions and information regarding the nature and course of symptoms, and a similar section was developed for the assessment of tic disorders. Also, a section was developed for the assessment of other proposed OCD-related conditions using DSM-IV criteria (Nestadt et al., 2000). Since PNB and PSP are not DSM-IV diagnoses, we modeled their criteria after those for trichotillomania (Bienvenu et al., 2000). Examiners also interviewed knowledgeable informants to obtain additional diagnostic information (Mannuzza et al., 1985). For subjects who had received psychiatric treatment, examiners obtained medical records and contacted treatment providers, if necessary. The examiners completed a narrative formulation for each case.

At each site, two expert diagnosticians independently reviewed materials and met to resolve disagreements regarding diagnoses or ages of onset. In the OCGS, JHU consensus diagnosticians also reviewed materials from other sites; we resolved disagreements before editing case materials and sending them for data entry.

Several diagnoses were assessed in both studies. Anxiety disorders include OCD itself, separation anxiety disorder (SAD), panic disorder (PD), agoraphobia, specific phobia (SpP), social phobia (SoP), and GAD. Personality disorders include obsessive-compulsive, avoidant (AvPD), and dependent (DPD). Putative “OCD spectrum” conditions include tic disorder (Tourette’s, chronic motor or vocal tic, or transient tic disorder), hypochondriasis, BDD, trichotillomania, PNB, PSP, PG, pyromania, kleptomania, anorexia nervosa (AN), bulimia nervosa (BN), alcohol dependence (AlD), and drug dependence (DD). Other Axis I conditions include major depressive disorder (MDD; including recurrent, rMDD), dysthymia (Dys), and bipolar disorder (BiD: Types I or II). Inter-rater reliabilities have been reported previously (Bienvenu et al., 2000, Nestadt et al., 2000, Nestadt et al., 2001, Samuels et al., 2006): for SAD, panic disorder, specific phobia, social phobia, GAD, hypochondriasis, BDD, PNB, PSP, MDD, dysthymia, and AlD, kappa values ranged from 0.6 to 1.0. Kappas were incalculable for agoraphobia, trichotillomania, AN, BN, PG, pyromania, kleptomania, and DD, but inter-rater agreement ranged from 96% to 100%. The intraclass correlation coefficient for obsessive-compulsive personality traits was 0.78.

Statistical analysis

We first compared demographic characteristics of case (OCGS) versus control (JHOFS) probands and first-degree relatives using chi-square or Fisher’s Exact tests. As shown in Table 2, there was some evidence for higher socioeconomic status in case versus control probands. Case relatives were more often in the lowest and highest age groups at interview, and there were non-monotonic relationships between case-control relative status and parents’ occupational status.

We next compared the lifetime prevalence of individual diagnoses in case versus control probands, using chi-square or Fisher's Exact tests. In addition, we calculated the difference in lifetime prevalence of individual diagnoses in cases and control probands, as well as the number needed to harm (NNH). NNH, calculated in the same way as the number needed to treat (Cook and Sackett, 1995), is recommended as an indication of the clinical importance of a variable (Kraemer et al., 2006). Here, NNH indicates how many persons would have to be sampled among those with OCD to have 1 more person with the individual comorbid diagnosis, compared to a sample of persons without OCD; lower NNH estimates indicate higher comorbidity. We calculated odds ratios, unadjusted and adjusted for potential demographic confounders, using logistic regression. In order to avoid overfitting, we included only those correlates of diagnoses that were also associated with case or control status ($p \leq 0.1$). [Lower education was associated with SpP, and higher education with BDD. SpP was associated with higher occupational status, and DD with lower occupational status. PD, SpP, SoP, and BN were associated with lower paternal occupational status.]

In the last set of analyses, we compared the lifetime prevalence of individual diagnoses in case versus control first-degree relatives, beginning as in the proband analyses. [SAD, PD, SoP, AvPD, DPD, tic disorder, hypochondriasis, BDD, trichotillomania, PNB, PSP, AN, BN, AlD, DD, MDD, rMDD, and Dys were associated with younger age. SpP, tic disorder, MDD, and AvPD were associated with higher maternal occupational status.] We performed two additional sets of logistic regression analyses with diagnoses for which there was evidence of higher prevalence in case versus control relatives. In the first set, we adjusted for proband diagnosis of the same individual disorder (to control for possible independent transmission of the disorder in these families); in the second, we adjusted for OCD in the relatives (to determine whether or not the disorder segregates independently of OCD in these families). All statistical tests were two-tailed.

Results

Proband (comorbidity) analyses

All of the anxiety disorders were statistically significantly associated with OCD (Table 3). Though GAD, PD, and agoraphobia were particularly strongly associated with OCD (high odds ratios or ORs), the lifetime prevalence of each of the anxiety disorders was substantially higher in OCD-affected than control probands (the difference in lifetime prevalence or DP ranged from 14% to 53%, corresponding to NNH estimates between 2 and 7). Cluster C personality disorders, esp. OCPD and AvPD, were also strongly associated with OCD, affecting 34% and 16% of OCD-affected probands, respectively (NNH = 4 and 7, respectively).

Tic disorders and the somatoform disorders hypochondriasis and BDD were also strongly associated with OCD, with substantial NNH estimates (5-8). PSP and trichotillomania were both strongly associated with OCD; PSP had a more substantial NNH estimate (4) than trichotillomania (10), the former affecting almost a third of OCD-affected probands. Neither eating disorder (AN or BN) nor the other impulse control disorders (PG, pyromania, or kleptomania) were common in case or control probands, and none of these conditions were

statistically significantly associated with OCD. Alcohol and drug dependence were common, but prevalences were similar in case and control probands.

All of the mood disorders were associated with OCD, and the unipolar conditions (esp. MDD and rMDD) had quite substantial NNH estimates (3-7), due to their high prevalence in case probands. Adjusting for demographic factors associated with case/control status and diagnosis (if applicable) did not appreciably affect the results.

First-degree relative (familiality) analyses

Familiality results largely mirrored those of the proband analyses, though with generally smaller odds ratios and larger NNH estimates (Table 4). Though a high prevalence of OCD was required in the relatives of OCD-affected probands by design (OCGS), we show results regarding OCD familiality at the top of Table 4. Of the anxiety disorders, agoraphobia and GAD were the most strongly familially related to OCD, though all of the anxiety disorders assessed except SpP had higher prevalences in case vs. control relatives. GAD was particularly common in case relatives, affecting almost one third (NNH=4). Cluster C personality disorders, especially OCPD and AvPD, were also familially related to OCD, the former affecting more than a fifth of case relatives (NNH=5).

Tic disorders; the somatoform disorders hypochondriasis and BDD; the grooming disorders trichotillomania, PNB, and PSP; and AN were more common in case vs. control first-degree relatives. Of these conditions, PSP had the lowest NNH estimate (8), and eating disorders the highest (54). None of the other impulse control disorders (PG, pyromania, or kleptomania) nor substance dependence conditions (AlD or DD) differed in prevalence in case vs. control relatives.

Unipolar depressive disorders were substantially more common in case vs. control relatives, and these conditions showed the lowest NNH estimates of the remaining conditions, esp. MDD (NNH 5-6). BiD was not significantly more common in case vs. control relatives.

Adjusting for potential demographic confounders and proband diagnosis of the same condition did not substantially affect the results; however, adjusting for the relative's diagnosis of OCD did substantially decrease OR estimates, suggesting that conditions familially related to OCD occur most commonly in relatives who themselves have OCD. Nevertheless, agoraphobia, GAD, OCPD, tic disorders, PSP, and MDDs remained significantly more common in case than control relatives when adjusting for all of these variables simultaneously.

Discussion

In this study, to our knowledge the largest OCD family study to date, we found that anxiety disorders, related personality disorders, several (but not all) putative OCD-related conditions (Hollander et al., 2008), and depressive disorders were more common in persons with OCD and their first-degree relatives. Thus, using comorbidity and familiality information, there is evidence supporting both grouping OCD with anxiety disorders, and grouping some additional conditions with OCD.

Anxiety disorders and related personality disorders

All of the anxiety disorders assessed except specific phobia showed elevated comorbidity and familiality with OCD. Thus, consistent with previous studies (Black et al., 1992, Fyer et al., 2005, Nestadt et al., 2001), anxiety disorders (esp. agoraphobia and GAD) appear an important part of a familial OCD spectrum. The converse is not necessarily true. Though Biederman et al. recently found significantly elevated prevalences of OCD in children of parents with panic disorder or GAD (Biederman et al., 2006), earlier studies did not find elevated prevalences of OCD in families of patients with PD, agoraphobia, or GAD [e.g., (Goldstein et al., 1994, Noyes et al., 1987)]. Nevertheless, many earlier studies employed outdated diagnostic methods with hierarchies no longer considered valid. On balance, we find little empirical support for separating OCD from other anxiety disorders in DSM-5.

Personality disorders from the “anxious cluster” (esp. OCPD) also showed elevated comorbidity and familiality with OCD. The comorbidity results are consistent with prior controlled studies (Black et al., 1993, Samuels et al., 2000, Torres and Del Porto, 1995), and the familiality results are consistent with our previous family study (Samuels et al., 2000). We view these results as further support that OCD should not be separated from other anxiety disorders in DSM-5. Alternatively, since OCPD in particular is highly comorbid with and familially related to OCD, this personality disorder could be considered OCD-related.

Putative OCD-related disorders

Tic disorders—Despite the fact that we excluded probands with Tourette’s disorder, tic disorders showed elevated comorbidity and familiality with OCD, consistent with previous studies (do Rosario-Campos et al., 2005, Grados et al., 2001, Jaisoorya et al., 2003, Pauls et al., 1995). Interestingly, OCD also appears to be an important part of the familial spectrum of Tourette’s disorder [e.g., (Pauls et al., 1991)]. Thus, OCD and tic disorders are strongly familially related, and, from this standpoint, it would be sensible to group these conditions together in DSM-5. Further support for categorizing tic disorders as OCD-related comes from a study of comorbidity in patients with OCD, social phobia, or panic disorder (Richter et al., 2003); in that study, tics were significantly more common in persons with OCD than in persons with the other anxiety disorders.

Hypochondriasis and body dysmorphic disorder—Hypochondriasis and BDD also showed elevated comorbidity and familiality with OCD, as in our previous study (Bienvenu et al., 2000). Others have also found elevated prevalences of hypochondriasis and BDD in persons with OCD (Jaisoorya et al., 2003). Conversely, a controlled study of comorbidity in patients with hypochondriasis showed elevated prevalences of OCD (and other anxiety disorders) (Barsky et al., 1992). In a controlled family study of hypochondriasis, anxiety disorders were relatively common in case relatives, but not OCD in particular (Noyes et al., 1997). It is not yet clear whether or not the diagnosis hypochondriasis will appear in DSM-5 (Dimsdale and Creed, 2009); however, it seems likely that hypochondriasis is highly comorbid with and familially related to other anxiety disorders besides OCD. Unfortunately, hypochondriasis has not typically been assessed in family studies of other anxiety disorders [e.g., (Biederman et al., 2006, Goldstein et al., 1994, Noyes et al., 1987)]. We know of

no controlled family studies of BDD, though it would be of interest to know whether its comorbid and familial relationships with OCD are bidirectional. Nevertheless, it seems reasonable to consider BDD an OCD-related condition on the basis of extant comorbidity and familiality data.

Grooming disorders—Consistent with our previous study (Bienvenu et al., 2000), grooming disorders showed elevated comorbidity and familiality with OCD. Only one of these conditions, trichotillomania, is a DSM-IV diagnosis, currently grouped with "other impulse control disorders not elsewhere classified." Unlike our previous study (Bienvenu et al., 2000), which had a smaller sample size, trichotillomania by itself showed elevated comorbidity and familiality with OCD in the current study. Other controlled studies have also shown elevated prevalences of trichotillomania in persons with OCD (Jaisoorya et al., 2003), including in comparison to persons with other anxiety disorders (Richter et al., 2003). Conversely, OCD also appears relatively common in families of probands with trichotillomania (Lenane et al., 1992, Schlosser et al., 1994). Thus, on the basis of extant comorbidity and familiality studies, it seems reasonable to consider trichotillomania OCD-related.

PSP by itself also showed elevated comorbidity and familiality with OCD. PSP has not been studied as extensively as trichotillomania, and it is not clear whether or not PSP should be considered particularly OCD-related or, more generally, anxiety-related (Cullen et al., 2001, Richter et al., 2003). In this study, PNB by itself was not particularly highly comorbid with OCD, but it was familially related to OCD. As with PSP, it is not clear whether PNB is more appropriately considered an OCD-related or an anxiety-related condition.

Eating disorders—Eating disorders were uncommon in patients with OCD, control probands, and their relatives. Thus, eating disorders do not appear to be an important part of the familial OCD spectrum. Our group and Black et al. came to similar conclusions in previous studies (Bienvenu et al., 2000, Black et al., 1994). Interestingly, though eating disorders do not appear particularly common in persons with OCD or their relatives, OCD appears very common in persons with eating disorders (esp. AN) and their family members [e.g., (Lilenfeld et al., 1998)]. Nevertheless, we conclude there is insufficient evidence to consider AN or BN OCD-related.

Other impulse control disorders not elsewhere classified—The other impulse control disorders not elsewhere classified (i.e., PG, pyromania, and kleptomania) were uncommon in patients with OCD, control probands, and their relatives. Thus, these conditions do not appear an important part of the familial OCD spectrum. These findings are consistent with previous studies (Bienvenu et al., 2000, Black et al., 1994). Like eating disorders, the NNH for other impulse control disorders was relatively high compared to other potential OCD-related conditions. Thus, it would seem sensible not to consider them particularly OCD-related in terms of comorbidty and familiality.

Substance use disorders—Neither AlD nor DD showed elevated comorbidity or familiality with OCD, consistent with previous studies (Fyer et al., 2005, Nestadt et al.,

2001). Thus, on the basis of comorbidity and familiality, there is little evidence that substance dependence is OCD-related.

Other psychiatric conditions

Mood disorders—Depressive disorders (MDD, rMDD, and Dys) showed elevated comorbidity and familiality with OCD. The findings for rMDD were similar to our previous study (Nestadt et al., 2001); however, unlike our previous study, rMDD was transmitted independent of OCD itself here. Similar to other anxiety disorders, OCD may share genetic causes with depressive disorders (Hettema, 2008).

Implications for DSM-5

Though comorbidity and familiality are just two of many potential validators of diagnostic groupings (Phillips et al., 2010, Stein et al., 2010), the current study offers guidance from these perspectives. First, since anxiety disorders are highly comorbid with OCD, and they appear to share familial influences with OCD, we feel it would be erroneous to remove OCD from the anxiety disorders section in DSM-5. Second, since several additional conditions are highly comorbid with and appear to share familial influences with OCD, we feel it would be sensible to consider these as OCD-related conditions, specifically OCPD, tic disorders, BDD, trichotillomania, and possibly PSP. Putting these findings together, our results lend credence to the recent proposal to include an “Anxiety and obsessive-compulsive spectrum disorders” chapter in DSM-5 (Phillips et al., 2010, Stein et al., 2010). Our results do not support the inclusion of some proposed OCD spectrum conditions in this chapter, specifically anorexia or bulimia nervosa, the impulse control disorders PG, pyromania, or kleptomania, or alcohol or drug dependence.

Implications for OCD genetics

Several conditions appeared to be “OCD equivalents” from a familial perspective; i.e., they “ran in the families” independently of OCD itself. Agoraphobia, GAD, OCPD, tic disorders, PSP, and MDD all shared this characteristic. Thus, including these other conditions as “affected” phenotypes may be a sensible alternative to OCD alone in future OCD gene-finding studies. Notably, the prevalences of BDD and trichotillomania were also elevated in the first-degree relatives of OCD-affected probands, though not statistically significantly so when adjusting for OCD in the relatives. Though statistical power was generally substantial because of the relatively large sample size here, it is difficult to “rule out” that these other conditions are not transmitted independently of OCD itself, since these conditions were relatively infrequent (i.e., statistical power was lower). Indeed, the OR point estimates for trichotillomania and BDD adjusting for OCD in relatives were higher than those for most of the conditions that unambiguously “ran in the families” independently of OCD. In addition, it is not clear that these conditions *should* segregate independently in families of OCD-affected probands, given the extent of comorbidity of these conditions in OCD-affected probands. That is, this may be an example of “overadjustment,” since it is not clear where the boundaries lie in nature.

Limitations

Several limitations should be acknowledged when considering the implications of the current study. First, the family study approach is a “broad-brush” method from which to extrapolate putative shared genetic causes; multivariable twin methods would be more direct, though such methods also involve certain assumptions. Second, in the OCGS, all families included OCD-affected probands, so examiners were aware that many of the participants would have OCD; nevertheless, OCD itself was not of interest here. Third, we did not assess all of the anxiety or putative OCD-related disorders; e.g., we did not assess post-traumatic stress disorder (PTSD) in the JHOFS. [In the OCGS, the PTSD lifetime prevalence was 12% in OCD-affected probands and 8% in their first-degree relatives.] Also, we only assessed compulsive hoarding in those with suspected OCD, and it would be of interest to determine whether or not “pure” compulsive hoarding (without other OCD symptoms) is familially related to OCD. Fourth, the JHOFS and the OCGS recruited participants through clinics, advertisements, and self-help groups, and the OCGS recruited participants with familial OCD (Nestadt et al., 2000, Samuels et al., 2006). Thus, it remains unclear the extent to which our results would generalize to persons with OCD (and their families) in the general population. Fifth, several of the conditions we considered were not common in case or control probands or their relatives, so statistical power was limited to detect differences between groups; nevertheless, using the metric of the NNH, it would be difficult to justify these conditions’ inclusion in an OCD familial spectrum. Sixth, unlike our original family study (Nestadt et al., 2000), case and control probands were not matched on demographic variables. We addressed this limitation by adjusting for potential demographic confounders, including age, sex, race, and socioeconomic status (as well as by excluding OCGS families in which the probands were younger than 18 years old). To adjust for potential age-related confounding (period at risk, recall bias, or cohort effects), we adjusted for age group, recognizing that these effects are often non-linear. Notably, adjustment for potential demographic confounders had little effect on the strength of associations.

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References

Barsky AJ, Wyshak G, Klerman GL (1992). Psychiatric comorbidity in DSM-III-R hypochondriasis. Archives of General Psychiatry 49, 101–108. [PubMed: 1550462]

Biederman J, Petty C, Faraone SV, Henin A, Hirshfeld-Becker D, Pollack MH, de Figueiredo S, Feeley R, Rosenbaum JF (2006). Effects of parental anxiety disorders in children at high risk for panic disorder: a controlled study. Journal of Affective Disorders 94, 191–197. [PubMed: 16753222]

Bienvenu OJ, Samuels JF, Riddle MA, Hoehn-Saric R, Liang KY, Cullen BA, Grados MA, Nestadt G (2000). The relationship of obsessive-compulsive disorder to possible spectrum disorders: results from a family study. Biological Psychiatry 48, 287–293. [PubMed: 10960159]

Bienvenu OJ, Stein MB (2003). Personality and anxiety disorders: a review. Journal of Personality Disorders 17, 139–151. [PubMed: 12755327]

Black DW, Goldstein RB, Noyes R, Blum N (1994). Compulsive behaviors and obsessive-compulsive disorder (OCD): lack of a relationship between OCD, eating disorders, and gambling. Comprehensive Psychiatry 35, 145–148. [PubMed: 8187479]

Black DW, Noyes R Jr., Goldstein RB, Blum N (1992). A family study of obsessive-compulsive disorder. Archives of General Psychiatry 49, 362–368. [PubMed: 1586271]

Black DW, Noyes R, Pfohl B, Goldstein RB, Blum N (1993). Personality disorder in obsessive-compulsive volunteers, well comparison subjects, and their first-degree relatives. American Journal of Psychiatry 150, 1226–1232. [PubMed: 8328568]

Carter AS, Pollock RA, Suvak MK, Pauls DL (2004). Anxiety and major depression comorbidity in a family study of obsessive-compulsive disorder. Depression and Anxiety 20, 165–174. [PubMed: 15643633]

Cook RJ, Sackett DL (1995). The number needed to treat: a clinically useful measure of treatment effect. British Medical Journal 310, 452–454. [PubMed: 7873954]

Cullen BA, Samuels JF, Bienvenu OJ, Grados M, Hoehn-Saric R, Hahn J, Liang K, Wellen D, Dees M, Riddle M, Nestadt G (2001). The relationship of pathologic skin picking to obsessive-compulsive disorder. Journal of Nervous and Mental Disease 189, 193–195. [PubMed: 11277358]

Dimsdale JE, Creed FH (2009). The proposed diagnosis of somatic symptom disorders in DSM-V to replace somatoform disorders in DSM-IV-A preliminary report. Journal of Psychosomatic Research 66, 473–476. [PubMed: 19446706]

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. American Journal of Medical Genetics, Part B, Neuropsychiatric Genetics 136, 92–97.

First M, Gibbon M, Spitzer R, Williams G (1996). Users Guide for the SCID. Biometrics Research Division, New York State Psychiatric Institute: New York, NY.

Fyer AJ, Lipsitz JD, Mannuzza S, Aronowitz B, Chapman TF (2005). A direct interview family study of obsessive-compulsive disorder: I. Psychological Medicine 35, 1611–1621. [PubMed: 16219119]

Goldstein RB, Weissman MM, Adams PB, Horwath E, Lish JD, Charney D, Woods SW, Sobin C, Wickramaratne PJ (1994). Psychiatric disorders in relatives of probands with panic disorder and/or major depression. Archives of General Psychiatry 51, 383–394. [PubMed: 8179462]

Grabe HJ, Ruhrmann S, Ettelt S, Buhtz F, Hochrein A, Schulze-Rauschenbach S, Meyer K, Kraft S, Reck C, Pukrop R, Freyberger HJ, Klosterkötter J, Falkai P, John U, Maier W, Wagner M (2006). Familiality of obsessive-compulsive disorder in nonclinical and clinical subjects. American Journal of Psychiatry 163, 1986–1992. [PubMed: 17074951]

Grados MA, Riddle MA, Samuels JF, Liang KY, Hoehn-Saric R, Bienvenu OJ, Walkup JT, Song D, Nestadt G (2001). The familial phenotype of obsessive-compulsive disorder in relation to tic disorders: the Hopkins OCD family study. Biological Psychiatry 50, 559–565. [PubMed: 11690590]

Hanna GL, Himle JA, Curtis GC, Gillespie BW (2005). A family study of obsessive-compulsive disorder with pediatric probands. American Journal of Medical Genetics, Part B, Neuropsychiatric Genetics 134, 13–19.

Hettema JM (2008). What is the genetic relationship between anxiety and depression? American Journal of Medical Genetics, Part C, Seminars in Medical Genetics 148C, 140–146. [PubMed: 18412101]

Hollander E, Braun A, Simeon D (2008). Should OCD leave the anxiety disorders in DSM-V? The case for obsessive compulsive-related disorders. Depression and Anxiety 25, 317–329. [PubMed: 18412058]

Jaisoorya TS, Reddy YC, Srinath S (2003). The relationship of obsessive-compulsive disorder to putative spectrum disorders: results from an Indian study. Comprehensive Psychiatry 44, 317–323. [PubMed: 12923710]

Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, Williamson D (1997). Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. Journal of the American Academy of Child and Adolescent Psychiatry 36, 1065–1069. [PubMed: 9256586]

Kraemer HC, Wilson KA, Hayward C (2006). Lifetime prevalence and pseudocomorbidity in psychiatric research. Archives of General Psychiatry 63, 604–608. [PubMed: 16754833]

Lenane MC, Swedo SE, Rapoport JL, Leonard H, Sceery W, Guroff JJ (1992). Rates of obsessive compulsive disorder in first degree relatives of patients with trichotillomania: a research note. Journal of Child Psychology and Psychiatry 33, 925–933. [PubMed: 1634595]

Lilenfeld LR, Kaye WH, Greeno CG, Merikangas KR, Plotnicov K, Pollice C, Rao R, Strober M, Bulik CM, Nagy L (1998). A controlled family study of anorexia nervosa and bulimia nervosa: psychiatric disorders in first-degree relatives and effects of proband comorbidity. Archives of General Psychiatry 55, 603–610. [PubMed: 9672050]

Mannuzza S, Fyer AJ, Endicott J, Klein DF (1985). Family Informant Schedule and Criteria. Anxiety Family Study Unit. New York State Psychiatric Institute: New York.

Mannuzza S, Fyer AJ, Klein DF, Endicott J (1986). Schedule for Affective Disorders and Schizophrenia - Lifetime version modified for the study of Anxiety disorders (SADS-LA): rationale and conceptual development. Journal of Psychiatric Research 20, 317–325. [PubMed: 3806426]

Nestadt G, Samuels J, Riddle M, Bienvenu OJ, Liang KY, LaBuda M, Walkup J, Grados M, Hoehn-Saric R (2000). A family study of obsessive-compulsive disorder. Archives of General Psychiatry 57, 358–363. [PubMed: 10768697]

Nestadt G, Samuels J, Riddle MA, Liang KY, Bienvenu OJ, Hoehn-Saric R, Grados M, Cullen B (2001). The relationship between obsessive-compulsive disorder and anxiety and affective disorders: results from the Johns Hopkins OCD Family Study. Psychological Medicine 31, 481–487. [PubMed: 11305856]

Noyes R Jr., Clarkson C, Crowe RR, Yates WR, McChesney CM (1987). A family study of generalized anxiety disorder. American Journal of Psychiatry 144, 1019–1024. [PubMed: 3605423]

Noyes R Jr., Holt CS, Happel RL, Kathol RG, Yagla SJ (1997). A family study of hypochondriasis. Journal of Nervous and Mental Disease 185, 223–232. [PubMed: 9114807]

Pauls DL, Alsobrook JP, Goodman W, Rasmussen S, Leckman JF (1995). A family study of obsessive-compulsive disorder. American Journal of Psychiatry 152, 76–84. [PubMed: 7802125]

Pauls DL, Raymond CL, Stevenson JM, Leckman JF (1991). A family study of Gilles de la Tourette syndrome. American Journal of Human Genetics 48, 154–163. [PubMed: 1985456]

Pfohl B, Blum N, Zimmerman M, Stangl D (1989). Structured Interview for DSM-IIIR Personality - SIDP-R. University of Iowa College of Medicine: Iowa City, IA.

Phillips KA, Stein DJ, Rauch S, Hollander E, Fallon B, Barsky A, Fineberg N, Mataix-Cols D, Ferrão YA, Saxena S, Wilhelm S, Kelly MM, Clark LA, Pinto A, Bienvenu OJ, Farrow J, Leckman J (2010). Should an obsessive-compulsive spectrum grouping of disorders be included in DSM-V? Depression and Anxiety 27, 528–555. [PubMed: 20533367]

Richter MA, Summerfeldt LJ, Antony MM, Swinson RP (2003). Obsessive-compulsive spectrum conditions in obsessive-compulsive disorder and other anxiety disorders. Depression and Anxiety 18, 118–127. [PubMed: 14625876]

Samuels J, Nestadt G, Bienvenu OJ, Costa PT, Riddle MA, Liang KY, Hoehn-Saric R, Grados MA, Cullen BA (2000). Personality disorders and normal personality dimensions in obsessive-compulsive disorder. British Journal of Psychiatry 177, 457–462.

Samuels JF, Riddle MA, Greenberg BD, Fyer AJ, McCracken JT, Rauch SL, Murphy DL, Grados MA, Pinto A, Knowles JA, Piacentini J, Cannistraro PA, Cullen B, Bienvenu OJ, Rasmussen SA, Pauls DL, Willour VL, Shugart YY, Liang KY, Hoehn-Saric R, Nestadt G (2006). The OCD Collaborative Genetics Study: Methods and sample description. American Journal of Medical Genetics, Part B, Neuropsychiatric Genetics 141, 201–207.

Schlosser S, Black DW, Blum N, Goldstein RB (1994). The demography, phenomenology, and family history of 22 persons with compulsive hair pulling. Annals of Clinical Psychiatry 6, 147–152. [PubMed: 7881494]

Stein DJ, Fineberg NA, Bienvenu OJ, Denys D, Lochner C, Nestadt G, Leckman JF, Rauch SL, Phillips KA (2010). Should OCD be classified as an anxiety disorder in DSM-V? Depression and Anxiety 27, 495–506. [PubMed: 20533366]

Storch EA, Abramowitz J, Goodman WK (2008). Where does obsessive-compulsive disorder belong in DSM-V? Depression and Anxiety 25, 336–347. [PubMed: 18412060]

Torres AR, Del Porto JA (1995). Comorbidity of obsessive-compulsive disorder and personality disorders: a Brazilian controlled study. Psychopathology 28, 322–329. [PubMed: 8838405]

van Grootheest DS, Cath DC, Beekman AT, Boomsma DI (2005). Twin studies on obsessive-compulsive disorder: a review. Twin Research and Human Genetics 8, 450–458. [PubMed: 16212834]

Table 1:

Prior controlled studies of lifetime prevalence (%) of other diagnoses in patients with OCD and/or their first-degree relatives

	N	DX	SAD	PD	Ag	SpP	SoP	GAD	OCPD	AvPD	DPD	TD	Hyp	BDD	TTM	PNB	PSP	AN	BN	MDD	rMDD	Dys	BiD	PG	Py	Kl	AlD	DD
Studies of Comorbidity																												
Black et al., 1993[a,b]	32 33	SIDPD (DSM-III)							**28**[*] 6	**22**[*] 0	**50**[*] 0																	
Torres and Del Porto, 1995 [a]	40 40	SIDP-R (DSM-III-R)							**18**[*] 0	**52**[*] 5	**40**[*] 5																	
Bienvenu et al., 2000 Samuels et al., 2000 Nestadt et al., 2001 Grados et al., 2001 [c]	80 73	SADS[e,f], SIDP-R (DSM-IV)	**18**[*] 4	**21**[*] 0	**17**[*] 1	31 17	36 21	**13**[*] 1	**32**[*] 6	**15**[*] 1	4 0	6[c] 0[c]	**15**[*] 0	**16**[*] 3	4 1	25 14	**24**[*] 6	9 3	4 1		**54**[*] 11	8 1	1 0	0 0	0 0	3 0	15 16	8 8
Jaisoorya et al., 2003	23 200	STOBS, SCID, SADS[f] (DSM-IV)										**39**[*] 12	**13**[*] 0	**3**[*] 0	**3**[*] 0			0 0	0 0					0 0		0 0		
Studies of Familiality																												
Black et al., 1992 Black et al., 1993 Black et al., 1994[a,b]	126 126	DIS, SIDPD (DSM-III)		2[c] 0	3[c] 2	8 5	3 2	**22**[*] 12	11 8	1 3	1 2							2[c] 0	2[c] 1	4 4		2 4	1 0	0 0				
Pauls et al., 1995 Carter et al., 2004 [a]	466 100	STOBS, DIS, SADS[e] (DSM-III-R)		9 4		8 5	1 1	16 11				**5**[*] 1								21 22								
Bienvenu et al., 2000 Samuels et al., 2000 Nestadt et al., 2001 Grados et al., 2001 [c]	343 300	SADS[e,f], SIDP-R (DSM-IV)	**13**[*] 5	**9**[*] 3	**4**[*] 1	25 21	23 20	**16**[*] 5	**12**[*] 6	2 1	2 0	**6**[c*] 2[c]	3 1	**4**[*] 1	1 0	11 9	7 4	1 1	1 1		**15**[*] 9	4 3	2 1	0 0	0 0	0 1	14 13	6 6

	N	DX	SAD	PD	Ag	SpP	SoP	GAD	OCPD	AvPD	DPD	TD	Hyp	BDD	TTM	PNB	PSP	AN	BN	MDD	rMDD	Dys	BiD	PG	Py	Kl	AlD	DD
Fyer et al., 2005 [a]	179 112	SADS[e] (DSM-IV)	7[+] 2	7[+] 2		25 26	30 27	6[+] 2				1[g] 0								32 26		16 12					21 **30**[*]	11 11
do Rosario-Campos et al., 2005 [d]	325 140	STOBS (DSM-IV)										**12**[*] 2[d]																

N = number of case (top) and control (bottom) probands (studies of comorbidity) or relatives (studies of familiality); DX = semistructured or structured diagnostic interview(s); SAD = separation anxiety disorder; PD = panic disorder; Ag = agoraphobia; SpP = specific phobia; SoP = social phobia; GAD = generalized anxiety disorder; OCPD = obsessive-compulsive personality disorder; AvPD = avoidant personality disorder; DPD = dependent personality disorder; TD = any tic disorder; Hyp = hypochondriasis; BDD = body dysmorphic disorder; TTM = trichotillomania; PNB = pathological nail biting; PSP = pathological skin picking; AN = anorexia nervosa; BN = bulimia nervosa; MDD = major depressive disorder; rMDD = recurrent major depressive disorder; Dys = dysthymia; BiD = bipolar disorder (I or II); PG = pathological gambling; Py = pyromania; Kl = kleptomania; AlD = alcohol dependence; DD = drug dependence; SIDPD = Structured Interview for DSM-III Personality Disorders; SIDP-R = Structured Interview for DSM-III-R Personality; SADS = Schedule for Affective Disorders and Schizophrenia; DIS = Diagnostic Interview Schedule; STOBS = Schedule for Tourette syndrome and Other Behavioral Syndromes; * indicates a statistically significantly higher prevalence in the case vs. control group, two-tailed $\alpha = 0.05$; + indicates a trend towards a difference in prevalence in the case vs. control group, p between 0.05 and 0.10; [a] control probands had no (or virtually no) known Axis I psychopathology; [b] case probands with panic disorder, agoraphobia, and/or eating disorders were excluded; [c] excluded probands with Tourette's disorder or schizophrenia; [d] control probands with OCD or tic disorders were excluded; [e] lifetime anxiety and f school-aged children versions; [g] Tourette's disorder

Table 2:

Demographic characteristics of case and control probands and first-degree relatives

demographic characteristics	probands					relatives				
	case (n=382)		control (n=73)		p *	case (n=974)		control (n=233)		p *
	n	%	*n*	%		*n*	%	*n*	%	
age at interview										
5-17 years	*0*	0	*0*	0	0.32	*125*	13	*18*	8	<0.0005
18-29 years	*105*	28	*17*	23		*141*	14	*40*	17	
30-39 years	*97*	25	*26*	36		*116*	12	*50*	22	
40-49 years	*111*	29	*17*	23		*137*	14	*41*	18	
50+ years	*69*	18	*13*	18		*454*	47	*84*	36	
sex										
male	*117*	31	*29*	40	0.13	*389*	40	*94*	40	0.91
female	*265*	69	*44*	60		*585*	60	*139*	60	
race										
white	*372*	98	*72*	99	1.0	*925*	96	*228*	98	0.25
other	*9*	2	*1*	1		*35*	4	*5*	2	
education										
did not complete high school	*29*	8	*7*	10	0.004	*229*	24	*47*	20	0.22
high school graduate	*26*	7	*14*	19		*116*	12	*39*	17	
some college	*121*	32	*14*	19		*233*	24	*63*	27	
college graduate	*136*	36	*29*	40		*229*	24	*48*	21	
advanced degree	*68*	18	*9*	12		*155*	16	*36*	16	
yearly household income										
$0-19,999	*52*	14	*11*	16	0.45	*81*	10	*15*	7	0.23
$20,000-39,999	*60*	17	*13*	19		*150*	18	*35*	17	
$40,000-59,999	*63*	18	*14*	20		*170*	21	*49*	24	
$60,000-79,999	*54*	15	*14*	20		*122*	15	*34*	17	
$80,000-99,999	*49*	14	*4*	6		*82*	10	*29*	14	
$100,000+	*81*	23	*13*	19		*212*	26	*42*	21	
highest occupational status										
unskilled or unemployed	*37*	10	*5*	7	0.06	*181*	19	*36*	16	0.38
skilled manual employee	*13*	4	*7*	10		*39*	4	*10*	4	
clerical/sales/technical employee	*127*	34	*22*	32		*269*	29	*78*	34	
administrator	*100*	27	*23*	33		*200*	21	*55*	24	
executive/professional	*97*	26	*12*	17		*244*	26	*53*	23	
father's occupational status **										
unskilled or unemployed	*33*	9	*5*	8	0.07	*109*	12	*20*	9	0.02
skilled manual employee	*51*	14	*13*	19		*144*	15	*33*	14	
clerical/sales/technical employee	*68*	18	*17*	25		*169*	18	*50*	22	
administrator	*79*	21	*18*	27		*210*	22	*70*	31	
executive/professional	*144*	38	*14*	21		*301*	32	*55*	24	

demographic characteristics	probands					relatives				
	case (n=382)		control (n=73)		p *	case (n=974)		control (n=233)		p *
	n	%	*n*	%		*n*	%	*n*	%	
mother's occupational status **										
unskilled or unemployed	*167*	45	*35*	52	0.21	*489*	52	*134*	58	0.02
skilled manual employee	*4*	1	*3*	4		*44*	5	*4*	2	
clerical/sales/technical employee	*111*	30	*17*	25		*221*	24	*38*	17	
administrator	*53*	14	*8*	12		*106*	11	*27*	12	
executive/professional	*39*	10	*5*	7		*78*	8	*26*	11	

* chi-square or Fisher's exact test

** parents' occupational status refers to the highest status when the participant was growing up

Table 3:

Lifetime prevalences of disorders in case (OCD-affected) and control probands

	Case probands[1] (n=382)		Control probands[2] (n=73)		χ^2/FE [3] p-value	DP[4]	NNH[5]	OR[6]	95% CI [7]	AOR[8]	95% CI
Diagnoses[9]	***n***	**%**	***n***	**%**							
separation anxiety disorder	*81*	23	*6*	8	0.006	14	7	**3.2**	*1.4-7.7*	**3.2**	*1.4-7.7*
panic disorder	*84*	23	*1*	1	<0.0005	21	5	**21**	*2.8-152*	**20**	*2.7-145*
agoraphobia	*67*	18	*1*	1	<0.0005	17	6	**15**	*2.1-113*	**15**	*2.1-113*
specific phobia	*164*	44	*21*	30	0.03	14	7	**1.8**	*1.0-3.2*	**2.5**	*1.3-4.7*
social phobia	*184*	50	*24*	34	0.01	16	6	**2.0**	*1.2-3.4*	**2.1**	*1.2-3.7*
generalized anxiety disorder	*198*	54	*1*	1	<0.0005	53	2	**83**	*11-602*	**83**	*11-602*
obsessive-compulsive personality disorder	*120*	34	*4*	6	<0.0005	28	4	**8.8**	*3.1-24*	**8.8**	*3.1-24*
avoidant personality disorder	*55*	16	*1*	1	0.001	14	7	**13**	*1.8-99*	**13**	*1.8-99*
dependent personality disorder	*17*	5	*0*	0	0.05	5	20	3.7	*0.5-28*		
any tic disorder	*68*	18	*0*	0	<0.0005	18	5	**16**	*2.1-115*	**16**	*2.1-115*
hypochondriasis	*44*	12	*0*	0	0.002	12	8	**9.7**	*1.3-72*	**9.7**	*1.3-72*
body dysmorphic disorder	*55*	15	*2*	3	0.005	12	8	**6.2**	1.5-26	**5.5**	*1.3-23*
trichotillomania	*42*	11	*1*	1	0.009	10	10	**9.0**	*1.2-67*	**9.0**	*1.2-67*
pathological nail biting	*67*	18	*10*	14	0.42	4	25	1.3	*0.6-2.8*		
pathological skin picking	*115*	31	*4*	6	<0.0005	26	4	**7.8**	*2.8-22*	**7.8**	*2.8-22*
anorexia nervosa	*26*	7	*2*	3	0.29	4	24	2.6	*0.6-11*		
bulimia nervosa	*27*	7	*1*	1	0.06	6	17	5.6	*0.7-42*		
major depressive disorder	*253*	67	*23*	32	<0.0005	35	3	**4.3**	*2.5-7.4*	**4.3**	*2.5-7.4*
recurrent major depressive disorder	*176*	46	*9*	12	<0.0005	34	3	**6.1**	*2.9-13*	**6.1**	*2.9-13*
dysthymia	*70*	19	*4*	5	0.005	14	7	**4.0**	*1.4-11*	**4.0**	*1.4-11*
bipolar disorder (I or II)	*43*	12	*2*	3	0.02	9	11	**4.7**	*1.1-20*	**4.7**	*1.1-20*
pathological gambling	*9*	2	*0*	0	0.37	2	41	1.8	*0.2-14*		
pyromania	*10*	3	*0*	0	0.38	3	37	2.0	*0.2-16*		
kleptomania	*11*	3	*0*	0	0.22	3	34	2.2	*0.3-17*		
alcohol dependence	*62*	17	*12*	17	0.96	0	−426	1.0	*0.5-1.9*		
drug dependence	*47*	13	*8*	11	0.74	1	70	1.1	*0.5-2.5*		

[1] OCD-affected probands

[2] non-OCD-affected probands

[3] chi-square or Fisher's exact test

[4] difference in prevalence between case and control probands

[5] number needed to harm

[6] crude (unadjusted) odds ratio

[7] 95% confidence interval

[9] all diagnoses = probable or definite; **bold** indicates odds ratios > 1.0 (two-tailed $p \leq 0.05$)

[8] odds ratio adjusted for demographic factors associated with case/control status and diagnosis (if applicable); underline indicates that a random control was assigned the diagnosis for calculation purposes

Table 4:

Lifetime prevalences of potential spectrum disorders in case (OCD-affected) and control first-degree relatives

	Case relatives[1] (n = 974)		Control relatives[2] (n = 233)		χ^2/FE [3] p-value	DP[4]	NNH[5]	OR [6]	95% CI [7]	AOR[8]	95% CI	AOR[9]	95% CI	AOR[10]	95% CI
Diagnoses[11]	***n***	**%**	***n***	**%**											
obsessive-compulsive disorder	*524*	55	*16*	7	<0.0005	48	2	**16**	*10-28*						
separation anxiety disorder	*140*	15	*13*	6	<0.0005	10	10	**3.0**	*1.6-5.4*	**3.2**	*1.8-6.0*	**2.8**	*1.5-5.2*	1.4	*0.7-3.0*
panic disorder	*118*	12	*10*	4	<0.0005	8	12	**3.1**	*1.6-6.0*	**3.4**	*1.8-6.7*	**2.7**	*1.4-5.4*	1.6	*0.7-3.3*
agoraphobia	*93*	10	*2*	1	<0.0005	9	11	**12**	*3.0-50*	**12**	*3.0-50*	**10**	*2.6-43*	**5.8**	*1.4-24*
specific phobia	*293*	31	*56*	24	0.05	6	15	1.4	*1.0-1.9*						
social phobia	*303*	32	*54*	23	0.01	9	12	**1.5**	*1.1-2.2*	**1.7**	*1.2-2.4*	**1.6**	*1.1-2.3*	1.0	*0.6-1.4*
generalized anxiety disorder	*303*	32	*9*	4	<0.0005	28	4	**11**	*5.8-23*	**12**	*5.8-23*	**8.0**	*4.0-16*	**4.2**	*2.0-8.8*
obsessive-compulsive personality disorder	*182*	22	*13*	6	<0.0005	16	6	**4.2**	*2.3-7.5*	**4.2**	*2.3-7.5*	**3.6**	*1.9-6.6*	**2.2**	*1.1-4.1*
avoidant personality disorder	*59*	7	*3*	1	0.002	6	17	**5.3**	*1.6-17*	**5.2**	*1.6-17*	**4.6**	*1.4-15*	1.6	*0.5-5.6*
dependent personality disorder	*19*	2	*0*	0	0.02	2	43	4.9	*0.6-37*						
any tic disorder	*137*	14	*5*	2	<0.0005	12	8	**7.5**	*3.0-18*	**6.9**	*2.7-18*	**5.8**	*2.2-15*	**2.8**	*1.0-7.8*
hypochondriasis	*42*	4	*3*	1	0.02	3	32	**3.5**	*1.1-12*	**4.3**	*1.3-14*	3.0	*0.9-10*		
body dysmorphic disorder	*60*	6	*2*	1	0.001	6	18	**7.8**	*1.9-32*	**8.6**	*2.1-36*	**6.9**	*1.6-29*	3.9	*0.8-18*
trichotillomania	*42*	4	*0*	0	0.001	4	22	**10**	*1.4-77*	**11**	*1.6-83*	**11**	*1.6-84*	5.9	*0.8-44*
pathological nail biting	*140*	15	*19*	8	0.01	6	15	**1.9**	*1.1-3.1*	**1.9**	*1.1-3.1*	**1.8**	*1.1-3.1*	1.3	*0.7-2.3*
pathological skin picking	*155*	17	*9*	4	<0.0005	13	8	**4.9**	*2.4-9.7*	**5.1**	*2.5-10*	**4.6**	*2.3-9.2*	**2.3**	*1.1-4.8*
anorexia nervosa	*26*	3	*2*	1	0.10	2	54	3.2	*0.8-14*	**4.4**	*1.0-19*	4.2	*1.0-18*		
bulimia nervosa	*15*	2	*2*	1	0.55	1	139	1.8	*0.4-8.1*						
major depressive disorder	*443*	46	*60*	26	<0.0005	20	5	**2.5**	*1.8-3.4*	**2.8**	*2.0-3.9*	**2.4**	*1.7-3.4*	**1.6**	*1.1-2.3*
recurrent major depressive disorder	*271*	28	*27*	12	<0.0005	17	6	**3.0**	*2.0-4.6*	**3.3**	*2.1-5.1*	**2.9**	*1.8-4.6*	**1.8**	*1.1-3.0*
dysthymia	*120*	13	*9*	4	<0.0005	9	12	**3.5**	*1.7-7.0*	**3.9**	*1.9-7.8*	**3.6**	*1.8-7.3*	2.0	*0.9-4.4*
bipolar disorder (I or II)	*39*	4	*4*	2	0.08	2	42	2.4	*0.9-6.9*						
pathological gambling	*11*	1	*0*	0	0.14	1	84	2.7	*0.3-21*						
pyromania	*6*	1	*0*	0	0.60	1	156	1.4	*0.2-12*						
kleptomania	*21*	2	*2*	1	0.29	1	74	2.6	*0.6-11*						
alcohol dependence	*119*	12	*31*	14	0.61	−1	−80	0.9	*0.6-1.4*						

Diagnoses[11]	Case relatives[1] (n = 974)		Control relatives[2] (n = 233)		χ^2/FE [3] p-value	DP[4]	NNH[5]	OR [6]	95% CI [7]	AOR[8]	95% CI	AOR[9]	95% CI	AOR[10]	95% CI
	n	%	*n*	%											
drug dependence	*58*	6	*15*	6	0.79	0	−210	0.9	*0.5-1.6*						

[1] first-degree relatives of OCD-affected probands

[2] first-degree relatives of non-OCD-affected probands

[3] chi-square or Fisher's exact test

[4] difference in prevalence between case and control relatives

[5] number needed to harm

[6] crude (unadjusted) odds ratio calculated using generalized estimating equations

[7] 95% confidence interval

[8] odds ratio calculated using generalized estimating equations, adjusted for demographic factors associated with case/control status and diagnosis (if applicable)…

[9] … and proband diagnosis of same disorder…

[10] …and OCD in relatives

[11] all diagnoses = probable or definite; **bold** indicates odds ratios > 1.0 (two-tailed $p \leq 0.05$); underline indicates that a random control was assigned the diagnosis for calculation purposes