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Differential Parental Influence in the Familial Aggregation of Obsessive Compulsive Disorder

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Abstract

The familial nature of OCD has been well established. Clinical characteristics such as early age of onset, comorbidity with tic disorders, and higher rates of symmetry symptoms have been associated with the familial aggregation of OCD, though little research has examined the differential impact of paternal and maternal OCD. The current study explored parental influence on the expression of these characteristics and reports on 310 probands diagnosed with OCD as well as 1,580 of their biological first-degree relatives. The probands were evaluated by trained clinical raters using semi-structured assessments, and relative diagnoses were obtained based on probands' reports. Similar to previous findings, 10.13% of the 1,580 relatives ($n = 160$) were reported to have significant OCD symptoms. Only probands who reported having a father with OCD, rather than any first-degree relative, were more likely to have an early age of onset, symmetry and exactness obsessions, and higher rates of comorbidity. No significant differences were found with respect to the probands who reported their mothers as having OCD. These findings suggest that paternal OCD, rather than simply any first-degree relative having OCD, may influence whether probands exhibit the clinical characteristics commonly associated with the familial subtype of OCD.

Keywords

obsessive-compulsive disorder; familial; subtype; paternal; anxiety

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1. Introduction

Obsessive-Compulsive Disorder (OCD) is a psychiatric condition characterized by recurrent intrusive thoughts (obsessions) and ritualistic behaviors (compulsions) that occur in approximately 2–3% of the general population (Karno, Golding, Sorenson, & Burnam, 1988). It is considered to be among the 10 most disabling medical conditions worldwide by the World Health Organization (Murray & Lopez, 1996) with 21% of cases beginning before age 10 (Kessler et al., 2005). The course of OCD is chronic (Eisen et al., 2013) and typically results in serious social and occupational impairment (Pinto, Mancebo, Eisen, Pagano, & Rasmussen, 2006). This is particularly true for those diagnosed with OCD at an early age (i.e., onset prior to 18 years of age), as they tend to exhibit more severe symptoms as well as more compulsive behavior (Geller et al., 1998; Stewart et al., 2004; Rosario-Campos et al., 2001). This has led many researchers to investigate genetic and familial factors that may increase the risk for developing early onset OCD.

Several twin and family studies have been conducted to examine the heritability of OCD. One adult twin study reports that genetics account for 33% and 26% of symptom transmission (obsessions and compulsions, respectively; Jonnal et al., 2000), while other studies estimate the heritability to be as high as 47% (Clifford, Murray, & Fulker, 1984). Family studies have consistently provided evidence that OCD occurs more frequently in the first degree relatives of OCD probands than in the general population (Nestadt et al., 2000; Pauls, Alsobrook, Goodman, Rasmussen, & Leckman, 1995) and a meta-analysis of five OCD family studies found the summary odds ratio (OR) of relatives of OCD probands having significant OCD symptoms to be 4.0 as compared to the relatives of controls (Hettema, Neale, & Kendler, 2001). In addition to finding a familial aggregation of OCD, Pauls et al. (1995) and Nestadt et al. (2000) showed that probands with higher rates of OCD among their relatives typically had an earlier age of onset. Remarkably, the family study by Nestadt et al. (2000) found that not a single case of OCD was reported in the relatives of probands diagnosed with late onset OCD (i.e., onset 18). Furthermore, the most recent multigenerational family clustering study designed to address many of the limitations of earlier research found that additive genetic factors account for 47% of the familial risk apart from environmental factors and that this risk is higher among probands diagnosed before age 18, though not significantly so (Mataix-Cols et al., 2013).

In addition to research suggesting that early onset OCD is familial, extant research suggests that early onset OCD is a sub-group with its own unique set of characteristics and comorbid presentation. Several studies have pointed to a higher incidence of tics and Tourette's disorder among those diagnosed with early onset OCD (Grados et al., 2001; Leonard et al., 1992; Chambane et al., 2005; Millet et al., 2004; Diniz et al., 2004; Janowitz et al., 2009). Research has also demonstrated that tics and Tourette's disorder occur more frequently among the first degree relatives of those diagnosed with early onset OCD (Grados et al., 2001; Geller et al., 1998; Pauls et al., 1995; Hanna, Himle, Curtis, & Gillespie, 2005) as well as higher rates of OCD among the family members of probands with comorbid OCD and Tourette's disorder (Chabane et al., 2005; Leonard et al., 1992). Such findings have led researchers to suggest that a bidirectional relationship exists between OCD and tics among the family members of OCD probands (Hanna et al., 2005).

Additional factors such as symptom presentation have been associated with the familial aggregation of OCD. Although only a small number of studies have examined familial transmission of specific symptoms, the available research points to a higher incidence of symmetry obsessions among those with familial OCD. Alsobrook, Leckman, Goodman, Rasmussen, and Pauls (1999) performed a segregation analysis indicating that relatives were at an increased risk for OCD when OCD probands scored higher for symmetry and ordering symptoms. Another study found that among early onset OCD probands with ordering compulsions, 45.4% of their first-degree relatives indicated definite or subthreshold OCD symptoms versus only 18.8% of the relatives of probands without ordering compulsions (Hanna et al., 2005). These findings suggest that early onset OCD may have a unique symptom presentation in addition to being comorbid with tic disorders.

Among other psychiatric illnesses, age of onset has been used to identify sub-groups with more severity, comorbidity, and greater heritability. For example, childhood onset schizophrenia has been associated with greater severity ratings (Gordon et al. 1994) and higher heritability compared to adult onset schizophrenia (Gorwood, Leboyer, Jay, Payan, & Feingold, 1995). Similar findings have been noted for bipolar disorder (Carter, Mundo, Parikh, & Kennedy, 2003; Somanath, Jain, & Reddy, 2002) leading researchers to suggest that early onset Bipolar disorder should be categorized as a specific subgroup of the disorder (Bellivier et al., 2003). In searching for factors that could increase the risk for developing these neuropsychiatric disorders, researchers have also begun investigating the role of advanced parental age, particularly with regard to the age of the father at the time of the proband's birth. It is suggested that advanced paternal age increases the likelihood of inheriting de novo spermatogonia mutations that place offspring at an elevated risk for developing schizophrenia (Byrne, Agerbo, Ewald, Eaton, & Mortensen, 2003; Malaspina et al., 2001), bipolar disorder (Frans et al., 2008), and autism spectrum disorders (Reichenberg et al., 2006). A recent study by Wu et al. (2012) found that advanced paternal age increased the relative risk of offspring developing OCD by an OR of 2.22 for father's aged 30–34 and an OR of 5.41 for father's older than 35. However, a recent multi-generational family aggregation study in Denmark identified advanced maternal age (OR = 1.25), rather than paternal age, as a significant risk factor for the development of OCD (Steinhausen, Bisgaard, Munk Jørgensen, & Helenius, 2013). These conflicting findings as to the role of parental age in the heritability of OCD warrant further investigation. Considering that early onset OCD is associated with the familial aggregation of OCD symptoms and advanced parental age could play a role in the heritability of the disorder, it is possible that advanced parental age may be a risk factor for the development of early onset OCD.

The purpose of this study is to further elucidate the clinical characteristics associated with the familial aggregation of OCD as well as to investigate the role of paternal versus maternal OCD in the development of early onset OCD symptoms. Consistent with previous research, we expected that patients with early onset OCD would be more likely have first degree relatives with significant OCD symptoms. We also predicted that the probands with relatives affected by OCD would demonstrate a higher prevalence of tic disorders as well as symmetry and ordering symptoms. In addition, we explored the association of parental age with early age of OCD onset to investigate possible increased risk associated with advanced parental age.

2. Method

2.1. Participants

The current study reports on 310 adult probands enrolled in the Brown Longitudinal Obsessive-Compulsive Study (BLOCS), a NIMH funded naturalistic prospective study on the course of OCD, as well as 1,580 of their biological first-degree relatives. Probands were included in the study if they had a primary DSM-IV diagnosis of OCD (i.e., OCD was the disorder that participants identified as causing the most problems over their lifetime), were at least 19 years old, had sought treatment for OCD within the past 5 years, and were willing and able to sign written consent. The only exclusion criterion was the presence of an organic mental disorder. Demographic and clinical characteristics of this sample are consistent with other OCD samples, including the DSM-IV field trial (Foa & Kozak, 1995; Rasmussen & Tsuang, 1986). A detailed description of the BLOCS sample, recruitment methods, and study procedures can be found elsewhere (Pinto et al., 2006).

2.2. Procedure

Participants were recruited from several psychiatric treatment settings in Rhode Island and Southeastern Massachusetts. Specific recruitment sites included a hospital-based outpatient OCD clinic, inpatient and partial hospitalization units of a private psychiatric hospital, two community mental health centers, three private practice psychotherapy sites specializing in OCD treatment, as well as a general outpatient psychiatric group practice. This study was approved by the Institutional Review Boards of Butler Hospital and Brown University. Once written informed consent was obtained, probands were interviewed directly by trained clinical interviewers at study intake. Family history data concerning each first-degree relative was collected at intake, and participants also completed a battery of self-report measures during the interviews.

2.3. Assessments

The Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (First et al., 1996) was used to establish diagnoses at intake. Demographic and clinical information was collected using the Butler Hospital OCD Database, a semi-structured rater-administered interview (Rasmussen, 1993). OCD symptoms and severity were evaluated using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), a reliable and valid 10-item rater-administered scale and the Y-BOCS Symptom Checklist (Goodman, Price, Rasmussen, Mazure, Delgado et al., 1989; Goodman, Price, Rasmussen, Mazure, Fleischmann et al., 1989). Axis I diagnoses and Y-BOCS total scores in this study have been found to have good to excellent interrater reliability as reported by Eisen et al. (2010).

Family history data concerning each biological first-degree relative were collected from the probands during the intake interview or subsequent follow-up interviews. The family history of OCD was obtained using a semi-structured family screening form. Probands were asked to consider each of their first-degree relatives and report their experience of obsessions, compulsions, the time occupied by their symptoms, as well as distress and impairment they perceived to be attributable to OCD. Interviewers made best-estimate diagnoses for the relatives of the probands based on DSM-IV criteria using the information provided by the

OCD probands. If a first-degree relative had ever been diagnosed with OCD or the proband described symptoms that appeared to meet key diagnostic criteria (i.e. duration, impairment or distress), a “definite” diagnosis was assigned. If a relative appeared to exhibit clear symptoms of OCD but key diagnostic criteria were unknown based on the proband’s report, the interviewer assigned them a “probable” diagnosis. If probands reported their relative to exhibit possible symptoms of a disorder but they were unsure of the diagnostic criteria, they were assigned a “possible” diagnosis, and if they reported no symptoms, “no” diagnosis was coded. In some cases probands could not provide enough information to make an informed decision regarding their relatives’ diagnoses, in which case interviewers regarded this as missing data ($n = 15$).

2.4. Statistical analysis

Data were analyzed using SPSS 21 (IBM Corp., 2011). Each hypothesis outlined above was tested for any first-degree relative, then separately for mothers and fathers. Age of onset was collected at three levels in this study; age at first appearance of symptoms, age when symptoms first began to interfere, and age of DSM-IV OCD onset. Early onset OCD was defined as clinical OCD onset (e.g., full DSM-IV criteria) prior to age 18. Although there is not a clear consensus regarding the age cutoff for early onset OCD, using a cutoff of prior to age 18 is supported by a number of research studies (Nestadt et al., 2000; Hanna et al., 2005; Mataix-Cols et al., 2013). For the purposes of the present investigation, first-degree relatives with a rating of “definite” or “probable” OCD (significant OCD symptoms) were included in analysis for comparison to those with only “possible” OCD or “no” OCD as reported by probands.

3. Results

Descriptive data of participant ratings of first-degree relatives’ OCD symptoms are presented in Table 1. Of the 1,580 first-degree relatives reported on by probands, 160 were reported to have significant OCD symptoms (10.13% of all relatives), among these were 38 mothers (12.26% of mothers) and 27 fathers (8.77% of fathers). The mean age of the proband sample at intake was 40.42 years ($SD = 12.86$), 97.7% were white, 21.3% had a high school education or less while 78.7% had at least some college or greater, and 54.5% of probands were female.

The relationship between early onset OCD and the likelihood of any first-degree relatives experiencing significant OCD symptoms was not significant ($\chi^2(1) = 0.76, p = .385$). When analyzed separately for mothers and fathers, no significant relationship was found for mothers ($\chi^2(1) = 2.20, p = .138$), but a significant relationship was found for fathers ($\chi^2(1) = 4.68, p = .031$), indicating a higher rate of significant OCD symptoms among fathers of OCD probands with early onset OCD. Post-hoc analyses comparing age of proband OCD onset among probands’ fathers with and without significant OCD symptoms revealed a significantly younger age of onset among probands whose fathers had OCD ($M = 14.67$ years, $SD = 7.11$) compared to those with fathers without OCD ($M = 18.95$ years, $SD = 10.06$), $t(302) = 2.16, p = .031$. No differences were found with respect to age of onset comparing probands’ mothers with ($M = 17.08$ years, $SD = 9.48$) and without ($M = 18.76$ years, $SD = 9.94$) significant OCD symptoms, $t(304) = 0.98, p = .328$. As shown in Table 2,

there were no significant differences in comorbidity rates in the probands, regardless of family history of OCD.

Probands with first-degree relatives with significant OCD symptoms were not found to have higher rates of tic disorders ($\chi^2(1) = 0.35, p = .555$); further, no significant relationship emerged between probands with tic disorders and relatives' OCD when looking at mothers ($\chi^2(1) = 0.95, p = .331$) or fathers ($\chi^2(1) = 0.32, p = .570$) separately. Post-hoc comorbidity analysis revealed that probands with a father with significant OCD symptoms had a significantly higher number of comorbid lifetime DSM-IV diagnoses ($M = 3.37, SD = 2.19$) compared to those whose fathers did not have significant OCD symptoms ($M = 2.48, SD = 1.77$), $t(29.4) = -2.06, p = .048$. No differences were found with respect to comorbidity comparing probands' mothers with ($M = 2.47, SD = 2.26$) and without ($M = 2.58, SD = 1.77$) significant OCD symptoms, $t(305) = 0.32, p = .748$.

The relationship between probands report of symmetry and exactness obsessions and the likelihood of any first-degree relative with significant OCD symptoms was not significant ($\chi^2(1) = 2.09, p = .352$). However, probands with fathers with significant OCD symptoms were significantly more likely to report symmetry and exactness obsessions ($\chi^2(1) = 6.39, p = .037$); no significant relationship was found with respect to mothers and probands reporting symmetry and exactness ($\chi^2(1) = 1.95, p = .384$).

Correlations between paternal age at the time of the probands birth and age of proband OCD onset ($r = -.08, p = .142$) and maternal age at the time of the probands birth and age of proband OCD onset ($r = .03, p = .345$) were not significant. Only a marginal relationship was found between father's age at the time of proband birth and the age of first OCD symptom interference in probands, $r = -.11, p = .060$.

4. Discussion

The goal of this study was to further elucidate the relationship between early onset OCD and the familial aggregation of the disorder in a large clinical sample of adults with primary OCD. Unlike previous research (Pauls et al., 1995; Nestadt et al., 2000), the rate of reported OCD among first-degree relatives was not found to be higher among early-onset probands. This result corroborates recent findings by Mataix-Cols et al. (2013) in which early-onset probands showed a non-significant elevated risk compared to adult-onset probands. However, when examining whether paternal or maternal OCD in particular was related to early onset symptoms in probands, paternal OCD was found to be significantly associated. Probands with early onset OCD reported higher rates of significant OCD symptoms among their fathers than those with later onset OCD. In addition, probands who reported having a father with OCD reported a mean age of onset nearly 4.5 years younger than those without a father exhibiting significant OCD symptoms. No significant difference in age of OCD onset was found with respect to probands with maternal OCD, indicating that the association between early onset symptoms and the familial aggregation of the disorder may be more strongly influenced by families in which the father exhibits OCD symptoms.

Previous research has suggested that the familial aggregation of OCD is associated with higher rates of tic disorders in OCD probands (Chabane et al., 2005; Hanna et al., 2005).

This study failed to replicate these findings. Probands who reported having at least one family member with OCD did not exhibit a higher rate of tic disorders than probands who denied having a first-degree relative with OCD. Likewise, the rate of tic disorders among probands did not increase when examining paternal and maternal OCD separately. This result may have more to do with the low frequency of tic disorders overall in our sample compared with other studies (e.g., 5.5% versus 43.9% current tic disorder at intake; Pinto et al., 2006 vs. Chabane et al., 2005). Despite this result, probands who reported paternal OCD were more likely to have a higher number of comorbid lifetime DSM-IV diagnoses, a finding typically associated with early onset OCD (Rosario-Campos et al., 2001). This may be a function of the relationship between paternal OCD and an early onset OCD subtype, as patients who fall into this subtype are more likely to exhibit higher rates of comorbidity.

Contrary to our hypothesis, no significant differences were found when examining the rate of symmetry and exactness symptoms in probands who reported having at least one relative with significant OCD symptoms compared to those with relatives without significant OCD symptoms. However, probands who reported having a father with OCD showed higher rates of symmetry and exactness obsessions compared to those who did not report paternal OCD. Thus, the clinical picture most often associated with familial OCD (e.g., early age of onset, higher comorbidity, symmetry symptoms) was found to be supported in the current study only for the probands who reported having a father with OCD. When examining the age of the father in relation to the probands' age of onset of symptoms, only a slight trend emerged (non-significant). Therefore, preliminary correlational data seems to suggest that advancing paternal age does not play an important role in the offspring's age of onset; however, further research is needed to answer this question.

There are important limitations to this study that should be noted. First, the relative's diagnoses were based on the probands' report rather than direct interviews. In addition, the probands' age of onset was established through retrospective reporting, and we did not collect data on family member age of onset or treatment history. Thus, both of these factors were subject to the probands' perception and memory biases and future studies should collect these data in child and adult samples using comprehensive, direct interviews with all first-degree relatives. The generalizability of this study is also limited given that our sample consisted of predominately Caucasian, treatment seeking individuals. A broader community sample is needed to increase the external validity of these findings. Despite these limitations, this is one of the first studies examining the influence of paternal and maternal OCD in the familial aggregation of OCD as well as the clinical implications of each.

This article addresses an important gap in the literature by further examining the differential role of first-degree relatives in the expression of factors associated with familial OCD. These preliminary findings suggest that paternal OCD specifically, rather than familial OCD in general, may influence whether probands exhibit early onset symptoms, higher rates of comorbidity, and symmetry and exactness obsessions. This finding, if supported by future research, may have important implications for advancing our understanding of developmental risk factors moderating these clinically-relevant variables. The etiological mechanism by which paternal OCD influences the expression of these characteristics remains unclear and should be a focus of subsequent investigations. Furthermore, previous

research examining the familial aggregation of OCD has been conducted on the assumption that having any first-degree relative with the disorder is sufficient. Therefore future research, as well as re-analysis of research using data from previous family samples, should focus on the differential parental influence in the development of OCD and the associated clinical characteristics. Identifying specific patterns of familial aggregation is not only important in delineating a familial subtype of OCD, but is critical in clarifying the etiological mechanisms involved in the development of this condition.

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Highlights

- Parental Influence in the transmission of characteristics related to OCD was examined.
- Paternal OCD is associated with earlier age of onset of OCD symptoms.
- Paternal OCD is associated with a greater number of comorbid diagnoses.
- Paternal OCD is associated with symmetry and exactness obsessions.
- These findings are specific to paternal rather than maternal OCD.

Table 1

Participant Ratings of First-Degree Relatives OCD Symptoms

	Mother (N = 310)		Father (N = 308)		Siblings (N = 650)		Offspring (N = 312)	
	N	%	N	%	N	%	N	%
OCD								
Definite	13	4.2	9	2.9	36	5.5	14	4.5
Probable	25	8.1	18	5.8	34	5.2	11	3.5
Possible	41	13.2	22	7.1	37	5.7	23	7.4
No	231	74.5	259	84.1	543	83.5	264	84.6

Table 2

Lifetime DSM-IV Comorbidity Rates for OCD Probands

	Full Proband Sample (N = 310)		Any First Degree Relative with Probable OCD (N = 112)		Fathers with Probable OCD (N = 27)		Mothers with Probable OCD (N=38)	
	N	(%)	N	(%)	N	(%)	N	(%)
Anxiety Disorders	173	(55.8)	59	(52.7)	16	(59.3)	18	(47.4)
Mood Disorders	230	(74.2)	83	(74.1)	20	(74.1)	25	(65.8)
Psychotic Disorders	9	(2.9)	2	(1.8)	0	(0.0)	1	(2.6)
Substance Use Disorders	61	(19.7)	27	(24.1)	8	(29.6)	8	(21.1)
Eating Disorders	29	(9.4)	12	(10.7)	2	(7.4)	4	(10.5)
Somatiform Disorders	26	(8.4)	14	(12.5)	5	(18.5)	6	(15.8)
Any Impulse Control Disorders	52	(16.8)	19	(17.0)	7	(25.9)	4	(10.5)
Any Tic Disorders	35	(11.3)	12	(10.7)	3	(11.1)	2	(5.3)

Note. There were no significant differences in rates of proband comorbidity regardless of family history of OCD.