



Familial occurrence of tic disorder, anxiety and depression is associated with the clinical presentation of obsessive compulsive disorder (OCD) in children and adolescents



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ABSTRACT

Obsessive compulsive disorder (OCD) is a neuropsychiatric entity. The aim was to explore the association of familial OCD, tics, anxiety, and depression with the presentation of OCD in offspring. To our knowledge, this is the first study examining the association of other familial psychiatric disorders with OCD in offspring.

A total of 198 families recruited to a Scandinavian multicenter treatment study participated. Characteristics of the child were assessed with standard measures. Family psychiatric disorders were assessed with two methods: a parent interview with open questions and a parent interview with specific questions concerning tics, depression, anxiety, and OCD.

A family history of OCD was described in 6% of the probands. No differences were observed between children who had relatives with OCD and children without familial occurrence of OCD. Familial tic disorder was associated with comorbid tics, externalizing disorders, repeating compulsions, and hoarding in the child proband. Familial anxiety was associated with internalizing disorders and comorbid tics, whereas familial depression was associated with somatic obsessions and hoarding in the proband.

Our study shows that familial occurrence of other psychiatric disorders is associated with differences in the clinical presentation. Identifying subtypes may have implications for our understanding of the etiology of OCD.

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1. Introduction

Obsessive-compulsive disorder (OCD) is a frequent disorder in

children, adolescents and adults with prevalence rates of 1–3% (Geller, Biederman, Jones, & Shapiro, 1998). The disorder shows considerable variety with regard to onset, symptom presentation, comorbidity, and treatment response (Sobin, Blundell, & Karayiorgou, 2000; Nestadt, Di, Riddle, & Grados, 2009; Rosario-Campos, Leckman, Mercadante, & Shavitt, 2001). This heterogeneity may be one of the reasons why causal etiological mechanisms have not yet been identified. Addressing this complexity, some investigators have sought to identify putative OCD subtypes (Nestadt et al., 2009; Rosario-Campos et al., 2001; Leckman, Grice, Boardman, & Zhang, 1997) based on phenotypic presentation,

Abbreviations: OCD, Obsessive compulsive disorder; NordLOTS, Nordic Long-term Obsessive-compulsive disorder Treatment Study; CBT, Cognitive Behavioral Therapy; SSRI, Selective Serotonin Reuptake Inhibitor; KSADS-PL, the Schedule for Affective Disorders and Schizophrenia for School-Age Children; CY-BOCS, Children's Yale-Brown Obsessive Compulsive Scale

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differences in sex distribution, family history of psychiatric disorder, symptom severity and age of onset. OCD is often associated with comorbid psychiatric disorders including tic disorders, anxiety disorders and depression. In a Swedish study from 2008, Ivarsson, Melin, and Wallin (2008) showed that comorbidities are very common in patients with OCD; 47% of the participants had neuropsychiatric disorders with tic disorders being the most common neuropsychiatric comorbidity in 27% of the participants. Tic disorders were seen more frequently in males. Moreover, anxiety was described in almost 40% of the participants and affective disorders in almost 25% (Ivarsson et al., 2008). The occurrence of comorbidity seems to be related to age of onset, and early-onset OCD has frequently been associated with comorbid tic disorder or Tourette syndrome (TS) (Rosario-Campos et al., 2001; Scahill, Kano, King, & Carlson, 2003). The occurrence of either OCD or TS is associated with the occurrence of the other disorder in patients as well as in first-degree relatives (Rosario-Campos, Leckman, Curi, & Quatrano, 2005). Furthermore, an increased occurrence of OCD, anxiety disorders, tic disorders and depression has been shown in families of children and adolescents with diagnosed OCD (Skriner, Freeman, Garcia, & Benito, 2016; Lenane, Swedo, Leonard, & Pauls, 1990).

OCD aggregates in families, which suggests that family members share genetic and environmental risk factors. Both family and twin studies point towards a strong genetic component. Family studies have shown an increased prevalence of OCD in the relatives of OCD proband in the order of 3–10%, a figure that is even higher (22.5%) in relatives of children and young adolescents with OCD (Wolff, Alsobrook, & Pauls, 2000; Pauls, Alsobrook, Goodman, & Rasmussen, 1995; Hanna, Himle, Curtis, & Gillespie, 2005). Twin studies confirm the hypothesis that genetic factors are important in relation to OCD. Thus, concordance rates are higher in monozygotic twins than in dizygotic twin, and a heritability reaching 33% and 26% has been suggested for obsessions and compulsions, respectively (Jonnak, Gardner, Prescott, & Kendler, 2000; Hudziak, van Beijsterveldt, Althoff, & Stanger, 2004). In a recent study, Davis, Yu, Keenan, and Gamazon (2013) examined the heritability and the genetic architecture of TS and OCD. They concluded that both TS and OCD are highly heritable, polygenic disorders and that there is some genetic overlap between these two disorders.

A few studies have compared family and sporadic subtypes of OCD. They suggest that the subtypes differ in their presentation. Hence, Hanna and colleagues (Hanna et al., 2005) showed that in the familial form probands significantly more often had ordering compulsions, aberrant grooming behaviors and anxiety disorders, especially phobic disorders. Likewise, Arumugham and colleagues (Arumugham, Cherian, Baruah, & Viswanath, 2014) showed that a family history of OCD was associated with early onset obsessions of contamination, hoarding and symmetry and compulsions of washing, ordering and repeating. Furthermore, a family history of OCD was associated with greater severity of OCD and longer symptom duration. Both studies conclude that the familial form may have distinctive clinical features that are not shared by the sporadic subtype. In a study with predominantly adult patients, Viswanath and colleagues (Viswanath, Narayanaswamy, Cherian, & Reddy, 2011) showed that the occurrence of ordering and cognitive compulsion and the absence of sexual obsessions could predict familial OCD. In addition, lifetime comorbidity of major depression and anxiety disorders and a greater duration of untreated illness predicted familial OCD.

OCD seems to be a disorder with strong heritability with potential overlap of different psychiatric disorders across the generations. Studies comparing familial and sporadic OCD suggest that familial OCD may influence the presentation of OCD in the probands both concerning phenotype, severity and duration of OCD and treatment response (Hanna et al., 2005; Arumugham

et al., 2014; Viswanath et al., 2011). Furthermore, familial OCD has been associated with an increased risk of comorbid anxiety and depression (Viswanath et al., 2011). Thus, familial OCD has been suggested to be phenotypically different from non-familial OCD; and the familial form could therefore be a putative subtype of OCD. Since other psychiatric disorders have been suggested to overlap in families (exemplified by TS and OCD), it also could be hypothesized that familial occurrence of other psychiatric disorders could influence the phenotypic presentation of OCD in the proband. Furthermore, the “early-onset” group might differ from the group with a later onset of symptoms.

To our knowledge, the potential association between the clinical presentation of OCD in children and adolescents and the occurrence of familial tic disorder, anxiety or depression remains unexplored. Therefore, we hypothesized, that psychiatric disorders in the families (OCD, tic disorders, anxiety and depression) are associated with specific phenotypic presentations of OCD in the offspring including age of onset, duration and severity of OCD, occurrence of comorbidity and the clinical presentation of OCD.

1.1. Aims

The aims of the present study were: (1) to describe the family occurrence of OCD, tic disorders, anxiety and depression in a Scandinavian population based on a large clinical cohort of children and adolescents with OCD and (2) to examine whether the occurrence of OCD and other psychiatric disorders in the family is associated with a specific phenotypic presentation of OCD in the child proband.

2. Materials and methods

All families included both in the Nordic OCD treatment Study (NordLOTS) and in a supplementary study at the Danish site were invited to participate in the present study. A total of 198 families accepted the invitation. The main study population ($n=167$, 62% of the eligible probands) was recruited from the NordLOTS study to which we added a continuously recruited, additional sample of 31 families ($n=31$, 78% of the eligible probands) from the Danish site. The latter sample has emerged as a side project to the NordLOTS study that evaluates the association with neuropsychiatric variables. The rationale, design and methods of the NordLOTS study were applied for both clinical samples and have been described in detail elsewhere (Ivarsson, Thomsen, Dahl, & Valderhaug, 2010; Thomsen, Torp, Dahl, & Christensen, 2013; Torp, Dahl, Skarphedinsson, & Thomsen, 2015). In brief, participants were recruited through referrals from community mental health centers, general practitioners and child mental health specialists to clinics in Denmark, Norway and Sweden. The primary inclusion criterion was OCD, according to the DSM-IV criteria, which was confirmed through The Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version (K-SADS-PL) (Kaufman, Birmaher, Brent, & Rao, 1997). Furthermore, a score above or equal to 16 points on the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) (24) was required for inclusion. Exclusion criteria included mental retardation (IQ below 70), disorders with higher treatment priority: autism, anorexia nervosa, major depression with suicidality that demanded treatment, and psychosis.

2.1. Measures

The K-SADS-PL is a semi-structured interview for diagnostic assessment of DSM-IV psychiatric disorders (Kaufman et al., 1997). The K-SADS-PL was used to confirm the diagnosis of OCD

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