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School of Medicine
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Doctorate in Psychiatry and Psychological Medicine

CLINICAL HETEROGENEITY OF OBSESSIVE-COMPULSIVE DISORDER IN CHILDREN AND ADOLESCENTS: TEMPORAL STABILITY AND TREATMENT OUTCOMES

Doctoral Thesis

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Thesis presented by Lorena Fernández de la Cruz

to obtain the grade of Doctor by the Universitat Autònoma de Barcelona

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Prof. David Mataix-Cols and Dr. Miquel Àngel Fullana Rivas certify that they have supervised and guided the doctoral thesis entitled "CLINICAL HETEROGENEITY OF OBSESSIVE-COMPULSIVE DISORDER IN CHILDREN AND ADOLESCENTS: TEMPORAL STABILITY AND TREATMENT OUTCOMES", presented by Lorena Fernández de la Cruz. They hereby assert that this doctoral thesis fulfils the requirements to be defended.

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A Manolo por su ejemplo.

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INDEX

LIST OF ACRONYMS

ADHD	Attention Deficit Hyperactive Disorder
ANOVA	Analysis of Variance
BDI-Y	Beck Depression Inventory for Youth
CBT	Cognitive Behavior Therapy
CGAS	Children's Global Assessment Scale
ChOCI	Children's Obsessive-Compulsive Inventory
CY-BOCS	Children's Yale-Brown Obsessive and Compulsive Scale
CY-BOCS-SC	Children's Yale-Brown Obsessive and Compulsive Scale Symptom Checklist
DIS-IV	Diagnostic Interview Schedule - IV
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition, Revised
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
DY-BOCS	Dimensional Yale-Brown Obsessive and Compulsive Scale
ERP	Exposure and Response Prevention
FAS	Family Accommodation Scale
GAS	Group A Beta-Hemolytic Streptococcus
IF	Impact Factor
OCD	Obsessive-Compulsive Disorder
OCI-R	Obsessions and Compulsions Inventory – Revised
OCPD	Obsessive-Compulsive Personality Disorder
ODD	Oppositional Deafiant Disorder
PANDAS	Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus
PI	Padua Inventory
POTS	Pediatric Obsessive-Compulsive Disorder Treatment Study
sd	Standard Deviation
SDQ	Strengths and Difficulties Questionnaire
SRI	Serotonine Reuptake Inhibitor
SSRI	Selective Serotonine Reuptake Inhibitor
Y-BOCS	Yale-Brown Obsessive and Compulsive Scale
Y-BOCS-SC	Yale-Brown Obsessive and Compulsive Scale Symptom Checklist

PROLOGUE

This thesis, submitted to obtain the degree of Doctor by the Universitat Autònoma de Barcelona, includes results from two independent studies. Both studies have been published in international peer-reviewed journals with a global impact factor (IF) of 6.708 (Thompson Reuters Web of Knowledge, Journal Citation Reports 2011) and are listed below:

- **Study 1:** Fernández de la Cruz, L., Micali, N., Roberts, S., Turner, C., Nakatani, E., Heyman, I., & Mataix-Cols, D. (2012). Are the symptoms of obsessive-compulsive disorder temporally stable in children/adolescents? A prospective naturalistic study. *Psychiatry Res,* in press. DOI: 10.1016/j.psychres.2012.11.033 [IF: 2.524].
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These manuscripts have been published over the last year and represent the culmination of the clinical and research training I have received at the King's College London, Institute of Psychiatry, as well as the National and Specialist Clinic for Children and Adolescents with Obsessive-Compulsive and Related Disorders at the Maudsley Hospital in London, United Kingdom.

Upon completion of my Psychology degree in 2004, and given my interest in child and adolescent psychology, I enrolled for the MSc in Psychiatry and Clinical Psychology in Children and Adolescents (2004 – 2006), led by Prof. Josep Toro, at the Hospital Clínic de Barcelona. It was during this program that I developed a special interest in OCD. After this period, I started my residency in Clinical Psychology at the Consorci Sanitari de Terrassa. During my three-year training (2007 – 2010), there were two events that would determine the course of my professional career. First, I started my PhD within the Department of Psychiatry and Forensic Medicine at the Universitat Autònoma de Barcelona (2008 – 2009). Second, I had the opportunity to work, for a three-month period (January – April 2010), as a visiting researcher in Prof. Mataix-Cols' OCD and Related Disorders Team at King's College London, Institute of Psychiatry. During this time, I was involved in a number of research projects, including a study that I would later present (June 2010) to obtain the Certificate of Research Proficiency (*Certificat de Suficiència Investigadora*) [study currently published: Pertusa, A., Fernández de la Cruz, L., Alonso, P., Menchón, J.M., & Mataix-Cols, D. (2012). Independent Validation of the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS). *Eur Psychiatry, 27,* 598-604].

After finishing my Clinical Psychology training, I was awarded a 2-year advanced training fellowship (2010 – 2012) by the Alicia Koplowitz Foundation, which enabled my return to the Institute of Psychiatry. During my time there, I was able to join Prof. Mataix-Cols' research team, and also the clinical team at the National and Specialist Clinic for Children and Adolescents with OCD and Related Disorders, led by Dr. Isobel Heyman at the time. My link with both the research and the clinical teams at the Maudsley gave me the opportunity to work on the studies that would result in the scientific publications included in the present thesis.

I believe the PhD experience has stimulated my interest in research and prepared me for the demands and responsibilities of this work. I am pleased to report my continued professional involvement with the teams that have made this dissertation possible. Together, we are currently focusing on studies to reduce inequalities and improve access to evidence-based treatments for children and adolescents in ethnic minorities who suffer from OCD.

Lorena Fernández de la Cruz

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List of other publications, not included in the thesis, co-authored by the PhD candidate:

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INTRODUC TION

1. INTRODUCTION

1.1. PEDIATRIC OBESSIVE-COMPULSIVE DISORDER

1.1.1. Diagnostic features and developmental aspects

Obsessive-Compulsive Disorder (OCD) is a psychiatric condition included in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5). The disorder is contained in a new chapter entitled *Obsessive-Compulsive and Related Disorders* along with Body Dysmorphic Disorder, Hoarding Disorder, Trichotillomania (Hair-Pulling Disorder), and Excoriation (Skin-Picking) Disorder (American Psychiatric Association, 2013; Phillips, Stein, et al., 2010).

Although pediatric OCD possesses some peculiarities that will be described in this chapter, it does not differ drastically from adult OCD in its phenomenological presentation (American Psychiatric Association, 2013). As with adults, OCD in children and adolescents is characterized by the presence of obsessions, compulsions, or, most commonly, a combination of these features. Obsessions in this context are defined as recurrent and persistent thoughts, urges, or images that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress. There are attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion). Examples of obsessions include unwanted thoughts or images of harming loved ones, intrusive thoughts of being contaminated, and morally or sexually repugnant thoughts (e.g., intrusive thoughts of behaving in a way that violates one's morals or runs counter to one's sexual preferences). In turn, compulsions are repetitive behaviors (e.g., repetitive hand washing, ordering, or checking) or mental acts (e.g., repetitive praying, counting, or thinking good thoughts to undo or replace bad thoughts) that the affected person feels driven to perform in response to an obsession. These behaviors or mental acts are intended to prevent or reduce anxiety or distress, or prevent some dreaded event or situation. However, they are not connected in a realistic way with what they are designed to neutralize and prevent, or are clearly excessive (Abramowitz, Taylor, & McKay, 2009; American Psychiatric Association, 2013). The DSM-5 specifies that young children may not be able to articulate the aims of these behaviors or mental acts (American Psychiatric Association, 2013). In the same way, children are less likely to hold insight into their condition, probably due to less developed cognitive abilities to make this judgment (Swedo, Rapoport, Leonard, Lenane, & Cheslow, 1989).

According to the DSM-5 (American Psychiatric Association, 2013), to make the diagnosis of OCD the obsessions or compulsions must be time-consuming (for example, take more than one hour per day) or cause clinically significant distress or impairment in the normal functioning of the individual. Also, in customary DSM fashion, a diagnosis of OCD can only be given once substance side effects, other general medical conditions, and alternative psychiatric disorders have been ruled out.

Similarly, in diagnosing OCD it is important to differentiate commonplace childhood rituals (e.g., avoiding cracks on the pavement) from compulsions (Abramowitz et al., 2009; Leckman & Bloch, 2008). Beginning around the second year of life, most children develop a variety of rituals, habits, routines, and preferences, some of which resemble the behaviors associated with OCD (Evans, Gray, & Leckman, 1999; Evans et al., 1997; Zohar & Felz, 2001). Gesell and colleagues (Gesell, 1928; Gesell & Ilg, 1974) observed that young children, particularly those around the age of 2½, begin to establish rigid routines that are believed to be useful to master the tasks of a specific developmental epoch such as feeding, toileting, and dressing, among others. These routines and habits require establishing mental representation of behavioral sequences and cognitive schemas for the way things "should be", and this type of ritualized behavior continues throughout development (see Leonard, Goldberger, Rapoport, Cheslow, & Swedo, 1990). In the context of normal developmental, these rituals tend to be transient and have a presumed role in mastering anxiety and enhancing one's socialization. Similarities between normal developmental and OCD rituals can be observed, such as having a need for things to be "just-right", counting or having lucky numbers, and structuring rituals around bedtime. In contrast, OCD rituals have a later mean age of onset than developmental rituals, are distressing if not performed, ego-dystonic, isolating, and incapacitating (Leonard et al., 1990; Swedo et al., 1989).

1.1.2. Prevalence and course of the disorder

OCD is considered one of the most common psychiatric disorders, with lifetime prevalence estimates ranging from 1 to 3% in the general population and 1-year prevalence rates ranging from 0.5 to 2.1% (Flament et al., 1988; Fontenelle, Mendlowicz, & Versiani, 2006; Ruscio, Stein, Chiu, & Kessler, 2010; Zohar, 1999). These numbers are comparable for adult as well as childhood and adolescent OCD (Rasmussen & Eisen, 1998; Valleni-Basile et al., 1994). Approximately one half of adult patients report illness onset before adulthood (Stewart et al., 2004), with adult studies indicating 21 as the average age of onset (Rasmussen & Eisen, 1992). Meanwhile, the average age of onset for pediatric samples is around 10 years of age (Flament et al., 1990; Thomsen & Mikkelsen, 1991). While studies in adulthood have shown equal prevalence between males and females, pediatric samples have shown male to female ratios of 2-3:1 in pre-pubertal onset OCD, with proportions switching to 1:1.35 in post-pubertal onset OCD (Leonard et al., 1992).

Onset of the disorder is usually gradual and symptom severity will generally change over time, often in response to life stressors (Mataix-Cols, Rauch, et al., 2002; Stewart et al., 2004). If untreated, the course of OCD tends to be chronic, often with waxing and waning of symptoms (Ravizza, Maina, & Bogetto, 1997; Skoog & Skoog, 1999). Some individuals have an episodic course, while a minority have a deteriorating course. Remission rates in untreated populations are low (e.g., 20% for those reevaluated 40 years later) (Skoog & Skoog, 1999). Interestingly, despite the development of new cases in adults, the prevalence rate between adults and children is approximately equal, suggesting that in many childhood cases remission is likely (Kalra & Swedo,

2009). This observation is consistent with a meta-analysis of long-term outcome studies in pediatric-onset OCD, which suggested that 40% to 59% of cases remit with proper treatment (Stewart et al., 2004). A rare prospective longitudinal study (Micali et al., 2010), which followed-up a cohort of children and adolescents into early adulthood, found that OCD persisted in 41% of cases. Approximately half of the participants in that study were still receiving treatment at follow-up, and about 50% felt a need for further treatment. Therefore, for a substantial proportion of patients, OCD is chronic and persists into adulthood.

1.1.3. Comorbidity

Seventy-five percent of adults and children with OCD have one or more comorbid psychiatric conditions (Fireman, Koran, Leventhal, & Jacobson, 2001). In adults, the most common comorbid conditions are anxiety disorders (e.g., social phobia) and unipolar mood disorders (e.g., major depressive disorder) (Torres et al., 2006). In addition, 36% of OCD patients report lifetime suicidal thoughts (Torres et al., 2011). In those with childhood-onset OCD, comorbidities are more likely to be behavioral conditions, especially attention deficit hyperactivity disorder (ADHD) or oppositional defiant disorder (ODD). Indeed, research in a pediatric sample indicated that the most common comorbid diagnoses were ADHD, major depressive disorder, tic disorders, and ODD (Leonard et al., 2001). However, where OCD onset occurs after puberty, the pattern of comorbidity is more likely to mirror the adult form (Mancebo et al., 2008).

Up to 30% of individuals with OCD have a lifetime tic disorder (American Psychiatric Association, 2013). Moreover, it has been suggested that some forms of OCD can be etiologically related to chronic tic disorders (Leonard et al., 1992). The tic-related subtype (in which OCD occurs in an individual with a lifetime history of a chronic tic disorder) may account for as many as 10–40% of OCD cases diagnosed in childhood or adolescence (Leckman et al., 2010). This subtype represents a highly familial condition with specific clinical characteristics, such as sensory phenomena (e.g., uncomfortable sensations in the body, just-right perceptions, sense of incompleteness) and a characteristic clinical course and outcome characterized by an early peak in obsessive-compulsive symptom severity at 12.5 years, followed by an increased likelihood of remission (Bloch, Peterson, et al., 2006). These tic-related cases may be less likely to respond to selective serotonin reuptake inhibitors (SSRIs) alone and more likely to benefit from SSRI augmentation with a neuroleptic (Bloch, Landeros-Weisenberger, et al., 2006; March et al., 2007; McDougle et al., 1993). A “tic-related OCD” specifier has been recently included in the DSM-5 to account for these specific features (American Psychiatric Association, 2013; Leckman et al., 2010).

1.1.4. Etiological factors

OCD has been shown to run in families with the rate of OCD among first-degree relatives of adult OCD probands being approximately twice that of control probands. This rate is increased 10-

fold in first-degree relatives of individuals with a pediatric OCD onset (Pauls, 2010). In the largest population-based, family study of OCD, the risk for the disorder among relatives of OCD probands was shown to increase proportionally to the degree of genetic relatedness. That is, the risk for first-degree relatives was significantly higher than that for second- and third-degree, and non-biological relatives (Mataix-Cols et al., 2013). Twin studies have further supported these findings, indicating that OCD is a moderately heritable condition and that environmental risk factors, not shared by family members, are as important as genetic factors in predisposing individuals to OCD (Mataix-Cols et al., 2013). Gene by environment interactions are likely and their study remains a substantial challenge for the future (Grisham, Anderson, & Sachdev, 2008).

OCD has also been linked to a disruption in the brain's serotonin system (López-Ibor & López-Ibor, 2003), in particular, hypersensitivity of post-synaptic serotonin receptors (Gross, Sasson, Chopra, & Zohar, 1998). Individuals with the disorder might have a specific dysfunction in the genes encoding for the serotonin transporter (5-HTT) and serotonin receptor (5HT2A); however, these issues have not been consistently identified (Greenberg et al., 1998; Saiz et al., 2008). Dysfunctions in the glutamatergic (Greist, Jefferson, Kobak, Katzelnick, & Serlin, 1995; Wu et al., 2013) and the dopaminergic (Camarena, Loyzaga, Aguilar, Weissbecker, & Nicolini, 2007) systems have also been suggested as relevant in the genesis of the disorder.

A convergence of data from neuropsychological, neuroimaging, and psychopharmacological studies have suggested that individuals with OCD are experiencing a dysfunction in the orbitofrontal cortex, anterior cingulate cortex, and striatum (Kang et al., 2003; Milad & Rauch, 2012; Radua & Mataix-Cols, 2009). Deficits in executive functions (i.e., higher-order cognitive functions, such as response-inhibition, set-shifting, planning, goal-directed behavior, sustained attention, maintenance of cognitive set, working memory, impulse-control, decision-making, and self-regulation), as well as visuospatial abilities and psychomotor functioning, have all been observed (Andres et al., 2007; Kuelz, Hohagen, & Voderholzer, 2004).

Some cases of childhood-onset OCD (and tic disorders) may be a consequence of post-infectious autoimmune processes, being the group A beta-hemolytic streptococcus (GAS) the one that has received more attention (Murphy, Kurlan, & Leckman, 2010). The model for GAS-mediated presentation of OCD involves subcortical (and cortical/cerebellar) inflammation induced by the cross-reaction between anti-streptococcal auto-antibodies and basal ganglia antigens (Dale, Heyman, Giovannoni, & Church, 2005). Such cases are grouped within a set of clinical conditions called Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection (PANDAS) (da Rocha, Correa, & Teixeira, 2008). In such cases, obsessive-compulsive symptoms are sometimes successfully treated with antibiotics, if the intervention occurs early in the course of the disorder (Swedo, Garvey, Snider, Hamilton, & Leonard, 2001). Research indicates that infection-related OCD might account for no more than 10% of early-onset cases (Trifiletti & Packard, 1999), suggesting that there are several causal pathways for acquiring the disorder.

1.1.5. Treatment

According to the available evidence (e.g., Eddy, Dutra, Bradley, & Westen, 2004; Foa et al., 2005; Gava et al., 2007; O'Kearney, Anstey, & von Sanden, 2006; Soomro, Altman, Rajagopal, & Oakley-Browne, 2008; Pediatric OCD Treatment Study (POTS) Team, 2004), effective treatments for OCD include cognitive-behavior therapy (CBT) involving exposure and response prevention (ERP) and serotonin reuptake inhibitors (SRIs). Both interventions are recommended in international treatment guidelines for health professionals (American Psychiatric Association, 2007; National Institute for Health and Clinical Excellence, 2005).

CBT for OCD requires the individual to gradually learn to tolerate the anxiety associated with not performing their ritualistic behavior (i.e., ERP). In treatment, the individual is exposed to systematic, repeated, and prolonged confrontations with stimuli that provoke anxiety and the urge to perform compulsive rituals, while being asked to refrain from performing these rituals. ERP aims to teach patients with OCD that their obsessional anxiety does not persist indefinitely, and that avoidance behavior and compulsive rituals are unnecessary for averting harm (Abramowitz et al., 2009).

In turn, SRIs are the recommended pharmacological treatment for OCD. In controlled trials among youth with OCD, clomipramine (DeVeaugh-Geiss et al., 1992) and the SSRIs fluvoxamine (Riddle et al., 2001), sertraline (March et al., 1998), and fluoxetine (Geller, Hoog, et al., 2001) have been found superior to placebo. The pediatric OCD pharmacotherapy literature is consistent with the much larger adult literature in revealing (a) little placebo effect, (b) a 30% to 40% reduction in OCD symptoms, and (c) clinically significant residual symptoms even after a medication trial of adequate dose and duration (Franklin & Foa, 2011). In adults, augmentation with antipsychotic medication has shown to significantly improve outcome in about a third of treatment-refractory patients with OCD (Bloch, Landeros-Weisenberger, et al., 2006; Dold, Aigner, Lanzenberger, & Kasper, 2013). In adolescents, the available data are notably scarcer, however preliminary evidence suggests that these augmentation strategies might also be efficacious in youth with treatment resistant OCD (e.g., Masi, Pfanner, Millepiedi, & Berloffa, 2010; Thomsen, 2004).

Studies directly comparing the relative and combined efficacy of ERP and SRIs have generally been methodologically complex and yielded ambiguous findings (Foa, Franklin, & Moser, 2002). Despite the absence of definitive empirical support for combined treatment over ERP alone, many professionals continue to advocate combined procedures as the treatment of choice for OCD. Franklin and Foa (2011) state that concomitant pharmacotherapy is not required for every patient to benefit substantially from ERP, but also that concomitant pharmacotherapy does not appear to inhibit ERP treatment response. Concomitant pharmacotherapy is often used in clinical practice to manage comorbid symptoms known to negatively impact ERP outcomes, such as depression and ADHD. However, optimal sequencing of these treatments has yet to be established empirically (Franklin & Foa, 2011).

1.2. HETEROGENEITY OF OBSESSIVE-COMPULSIVE DISORDER

Symptoms of OCD are remarkably heterogeneous, to the extent that two patients with this diagnosis can display completely different, non-overlapping symptom patterns (Mataix-Cols, Rosario-Campos, & Leckman, 2005). This clinical heterogeneity is manifested similarly among pediatric and adult samples, although some differences have been described. For example, Geller et al. (2001) found that, compared with OCD adults, children and adolescents with OCD more often had obsessive fears of loss or harm to loved ones or self, as well as increased rates of hoarding/saving compulsions. Unique sex differences in the distribution of OCD symptoms have also been found in pediatric samples. For example, Mataix-Cols, Nakatani, Micali, and Heyman (2008) found that boys with OCD experienced more sexual obsessions whereas girls manifested more hoarding behavior. In this sample, contrary to adult studies, contamination-related OCD symptoms were not more frequent in girls, but distributed evenly between genders.

Factor analyses both in pediatric and in adult OCD populations have been used to group symptoms of OCD into several symptom dimensions that may better account for its heterogeneity. A meta-analysis of these studies by Bloch, Landeros-Weisenberg, Rosario, Pittenger, and Leckman (2008) identified four robust symptom dimensions: 1) *Hoarding*, which contained hoarding obsessions and compulsions; 2) *Symmetry*, which contained symmetry obsessions and ordering, repeating, and counting compulsions; 3) *Forbidden thoughts*, which contained aggressive, sexual, religious, and somatic obsessions; and 4) *Cleaning*, which contained contamination obsessions and cleaning compulsions. This meta-analysis involved 21 factor analytic studies including 5,124 participants. Four of these studies used a pediatric sample, totaling 679 participants (Delorme et al., 2006; Mataix-Cols et al., 2008; McKay et al., 2006; Stewart et al., 2007). In the meta-analysis, the only differences between the factor structures in regard to the adult and child samples were 1) that checking compulsions loaded highest on the *Forbidden Thoughts* factor in adults and on the *Symmetry* factor in children and 2) that somatic obsessions loaded highest on the *Forbidden Thoughts* factor in adults and on the *Cleaning* factor in children (Bloch et al., 2008).

The clinical heterogeneity of the disorder has raised the question of whether OCD is also etiologically heterogeneous. In answer, a multidimensional model has been proposed (Mataix-Cols et al., 2005) in which OCD would be considered a set of potentially overlapping syndromes rather than a unitary entity. Some of the etiological factors underpinning these related syndromes would be specific to each dimension, whereas some other etiologic factors would be common to all. If this model is accurate, then taking into account this phenotypic heterogeneity would improve understanding of the disorder's causes (Mataix-Cols et al., 2005). Moreover, this information would help us develop better and more specific treatments for the disorder.

A growing body of scientific data supports the validity of this approach. The evidence comes primarily from 1) clinical studies showing the phenotypically different presentation of the disorder (e.g., Leckman et al., 1994; Rosario-Campos et al., 2001); 2) developmental studies that have found an early emergence of specific behaviors that resemble the symptom dimensions

observed in OCD patients (e.g., Evans et al., 1999; Evans et al., 1997; Zohar & Felz, 2001); 3) longitudinal studies showing that OCD symptom dimensions are temporally stable (see Section *1.2.1. Temporal stability of the OCD symptom dimensions* below); 4) genetic studies relating different symptom dimensions with different patterns of genetic transmission (e.g., Iervolino, Rijsdijk, Cherkas, Fullana, & Mataix-Cols, 2011; Katerberg et al., 2010); 5) neuroimaging studies showing that different dimensions are mediated by partially distinct neural systems (e.g., Gilbert et al., 2009; Mataix-Cols, Wooderson, et al., 2004; van den Heuvel et al., 2009); and 6) treatment studies showing that response to CBT or SRIs varies across dimensions (e.g., Mataix-Cols, Marks, Greist, Kobak, & Baer, 2002; Mataix-Cols, Rauch, Manzo, Jenike, & Baer, 1999; Rufer, Fricke, Moritz, Kloss, & Hand, 2006).

As might be expected, the majority of research concerning the heterogeneity of OCD has been gathered from adult studies. More research is needed to test whether the validity of the assumptions of the so called "multidimensional model" may also be appropriate for the pediatric population (Mataix-Cols et al., 2005).

1.2.1. Temporal stability of the OCD symptom dimensions

The validity of the described symptom-based classification of OCD would be compromised if these symptom dimensions or clusters were not temporally stable; that is, if the content of the patients' symptoms dramatically changed over time (Fullana et al., 2007). While it is often assumed that OCD patients' symptoms fluctuate both in severity and content, to date only a handful of longitudinal studies (described in **Table 1**) have empirically examined this important question using modern psychometric instruments.

Studies in adults, both in clinical (Mataix-Cols, Rauch, et al., 2002; Rufer, Grothusen, Mass, Peter, & Hand, 2005) and in non-clinical samples (Fullana et al., 2009; Fullana et al., 2007; Novara et al., 2011) have shown that OCD symptom dimensions are temporarily stable. For example, Mataix-Cols et al. (2002) completed a prospective study of adult OCD patients who were repeatedly administered the Yale-Brown Obsessive and Compulsive Scale Symptom Checklist (Y-BOCS-SC) over a period of 2 years. In the majority of the cases, the patients maintained their symptoms across follow-up, and the strongest predictor of having a particular symptom was having had that symptom in the past.

In contrast, the very few studies evaluating the stability of the obsessive-compulsive symptoms and symptom dimensions in the children and adolescent population have shown inconclusive results. For example, Rettew, Swedo, Leonard, Lenane, and Rapoport (1992) found that in a sample of 73 children and adolescents with OCD no patient maintained the same constellation of symptoms from baseline to follow-up carried out 2 to 7 (mean 4.1 ± 1.3) years later. However, the study acknowledged that these changes could have occurred within (rather than between) symptom categories. In turn, Delorme et al. (2006) presented the results of a group

of pediatric patients followed for a mean length of 3.8 years and concluded that most of the dimensions were unmodified across time. As in adult clinical samples, OCD symptom dimensions in children appeared to remain essentially unmodified with changes from one dimension to another being rare. Of note, these assumptions are based on studies with a number of methodological limitations, including small sample sizes. Hence, further studies are needed to examine the temporal stability of symptom dimensions over the course of development.

Table 1. Published studies on the stability of the OCD symptoms and symptom dimensions.

Study	Sample	Length of the follow-up (mean years)	Assessment tool	Symptom Categories/Dimensions
Rettew et al. (1992)	73 children with OCD	7.9 years	Y-BOCS-SC	*Obsessions:* Aggressive, Contamination, Sexual, Hoarding/Saving, Religious, Symmetry/Exactness, Somatic, and Miscellaneous. *Compulsions:* Cleaning/Washing, Checking, Repeating, Counting, Ordering/Arranging, Hoarding/Collecting, and Miscellaneous.
Mataix-Cols, Rauch, et al., (2002)	117 adults with OCD	2 years	Y-BOCS-SC	Symmetry/Ordering, Hoarding, Contamination/Cleaning, Aggressive/Checking, Sexual/religious.
Rufer et al. (2005)	43 adults with OCD	6.1 years	Y-BOCS-SC	Symmetry/Ordering, Hoarding, Contamination/Cleaning, Aggressive/Checking, Sexual/religious.
Delorme et al. (2006)	42 children with OCD	3.8 years	Y-BOCS-SC	Symmetry/Ordering, Obsessive, Contamination/Cleaning, and Hoarding.
Fullana et al. (2007)	132 non-clinical adults	2 years	OCI-R	Washing, Checking, Ordering, Hoarding, Obsessing, and Neutralizing.
Fullana et al. (2009)	972 non-clinical adults	6 years	DIS-IV	Contamination/Washing, Harm/Checking, Symmetry/Ordering, and Shameful Thoughts.
Novara et al. (2011)	61 non-clinical adults	5 years	PI	Impaired Mental Control, Contamination, Checking, and Impulses and Impaired Motor Activity

Note: OCD Obsessive-Compulsive Disorder; Y-BOCS-SC Yale-Brown Obsessive Compulsive Scale – Symptom Checklist; OCI-R Obsessive-Compulsive Inventory – Revised; DIS-IV Diagnostic Interview Schedule IV; PI Padua Inventory.

Assessing the stability of OCD in a larger pediatric sample would facilitate an improved understanding of the disorder's progression, which is invaluable to parents and patients and also clinicians to help them discern what to expect in terms of outcome. Furthermore, if symptom dimensions were showed to be stable, then this would add to the literature supporting the multidimensional nature of OCD (Mataix-Cols et al., 2005).

1.2.2. Sexual obsessions in children and adolescents with OCD

Sexual obsessions are common in OCD and particularly debilitating. Both in pediatric and adult samples, factor analyses have found that these obsessions consistently load highly onto the *Forbidden thoughts* dimension (Bloch et al., 2008). This category, also known as unacceptable/taboo thoughts (Brakoulias et al., 2013; Pinto et al., 2007), also comprises aggressive and religious obsessions.

Sexual obsessions may include unwanted sexual thoughts about having sex with family members or children, fears about engaging in sexually aggressive behavior, thoughts of sex with animals, or concerns about sexual orientation (Grant et al., 2006; Williams & Farris, 2011). Sexual obsessions tend to be concealed symptoms that may remain undiagnosed because sufferers are often embarrassed to disclose their symptoms which might be perceived as unacceptable (Baer, 2001). In spite of this, they have shown to be common in OCD. In the national comorbidity survey replication study, 30.2% of adult people with OCD reported sexual and/or religious obsessions (Ruscio et al., 2010), although it is not known exactly how many of these experienced sexual obsessions since the two categories were combined. Similarly, Mataix-Cols et al. (2008) found that the prevalence of lifetime sexual obsessions in a sample of 236 children with OCD was 28%. Some reports have suggested that sexual obsessions are more common in adolescents and adults rather than in younger population with OCD (Geller, Biederman, et al., 2001).

Grant and colleagues (2006) studied a sample of 293 adult patients with OCD. One quarter of the sample reported a history of sexual obsessions, and 13.3% reported current sexual obsessions. They were more common in men and, as could be expected, were associated with the presence of other obsessive thoughts from the *Forbidden thoughts* dimension (i.e., aggressive and religious obsessions). Participants with sexual obsessions also reported a significantly earlier age of OCD onset as well as an earlier age of first treatment for OCD, relative to participants without sexual obsessions. In other studies, the presence of shameful thoughts (including sexual obsessions) has been associated with higher rates of help-seeking behavior, suggesting higher levels of associated distress (Fullana et al., 2009).

Generally, individuals with unacceptable thoughts, including sexual obsessions, have often been described as more treatment resistant than those with other types of OCD symptoms (Williams, Mugno, Franklin, & Faber, 2013). Some studies have associated this group with poorer response to treatment, both with CBT (Alonso et al., 2001; Mataix-Cols, Marks, et al., 2002; Rufer et al., 2006) and SRIs (Alonso et al., 2001; Shetti et al., 2005), as well as indicating that these patients require treatment for a longer period of time (Grant et al., 2006). Relatedly, Alonso et al. (2001) reported a trend towards fewer past treatments and a longer history of OCD symptomatology in patients with sexual or religious obsessions. Other studies, meanwhile, have not shown poorer treatment outcomes among individuals with sexual obsessions (Denys, Burger, van Megen, de Geus, & Westenberg, 2003; Erzegovesi et al., 2001; Mataix-Cols et al., 1999; Stein, Andersen, & Overo, 2007).

These mixed results do not clarify whether sexual obsessions are, in fact, more resistant to treatment or whether there are alternative causes underlying this diversity of treatment outcomes. For example, ERP in this group may be more challenging to implement given that compulsions associated with these obsessions tend to be primarily mental and reassurance-seeking behaviors may be easily overlooked as rituals (Williams et al., 2011). Additionally, the cues that prompt obsessions may be difficult to identify and access, limiting the ability of clinicians to develop effective exposures. As a result, treatment in this group is likely to require more exposures in imagination, and ritual prevention will need to include the suppression of mental compulsions, which are more difficult to monitor (Gillihan, Williams, Malcoun, Yadin, & Foa, 2012).

To date, sexual obsessions have remained largely unexplored in children and adolescents. This fact, along with the mixed treatment outcomes that have been found when symptoms from this category are present, leaves room and reason for a comprehensive and methodologically sound examination of this particular symptom presentation in a large sample of pediatric OCD patients. Such a study would enable a better understanding of these symptoms and will provide much-needed recommendations on how to approach such cases in clinical practice.

1.3. AIMS AND HYPOTHESES

The global aim of this research was to study unexplored clinical features of pediatric OCD taking into account the clinical heterogeneity of the disorder, using a large sample of patients referred to a national and specialist clinic in London, United Kingdom. In particular, we aimed to study the temporal stability of OCD symptoms and symptom dimensions (*Study 1*), as well as the nature of sexual obsessions (*Study 2*), a common and particularly disturbing presentation of OCD, in a pediatric OCD sample.

The specific aims of the included studies, as well as the hypotheses, are described below. The scientific publications derived from *Study 1* and *Study 2* will then be presented in *Chapter 2*.

Specific aims

Study 1:

- To establish the temporal stability of OCD symptoms and symptom dimensions over an average follow-up period of 5 years.
- To establish the impact of additional variables, such as the OCD age of onset or the severity of the symptoms, on the stability of the symptom dimensions.

Study 2:

- To establish the prevalence of sexual obsessions in a large clinical cohort of children and adolescents with OCD.

- To examine the demographic and clinical characteristics of children and adolescents with sexual obsessions.
- To examine the treatment outcomes of patients with vs. without sexual obsessions.

Hypotheses

Study 1:

1. In general, symptom categories and symptom dimensions would show temporal stability over time similar to that observed in adult samples.
2. Endorsing a symptom dimension at baseline would be the strongest predictor of endorsing that corresponding dimension at follow-up.
3. Symptom dimensions would remain stable when controlling for treatment effects (as changes in symptom dimensions could be confounded with overall reduction in OCD severity attributable to the intervention).

Study 2:

1. Sexual obsessions would be a common symptom in the sample, and would be more prevalent in adolescents than in younger children.
2. Patients with sexual obsessions would also present with other symptoms from the same dimension (aggressive and religious thoughts). Also, individuals with sexual obsessions would be more depressed than their counterparts who do not endorse sexual obsessions.
3. The presence of sexual obsessions would not be associated with poorer treatment outcome, as long as treatment is delivered by a specialist team and adapted to the developmental needs of the child.

SCIENTIFIC PUBLICATIONS

2. SCIENTIFIC PUBLICATIONS

2.1. STUDY 1: Temporal stability of the OCD symptoms in children and adolescents

Fernández de la Cruz, L., Micali, N., Roberts, S., Turner, C., Nakatani, E., Heyman, I., & Mataix-Cols, D. (2012). **Are the symptoms of obsessive-compulsive disorder temporally stable in children/adolescents? A prospective naturalistic study.** *Psychiatry Res*, in press. DOI: 10.1016/j.psychres.2012.11.033.

2.1.1. Background

OCD is a remarkably heterogeneous condition. This phenotypic heterogeneity is thought to reflect etiological heterogeneity. Factor analyses have consistently grouped OCD symptoms into several dimensions, which differentially correlate with various biological and clinical characteristics. In adults, the content of these symptom dimensions has demonstrated temporal stability, although this has largely been overlooked in pediatric samples and such limited studies are hampered by methodological weaknesses. Moreover, developmental factors may play a role in the stability of the symptoms across childhood and adolescence. We aimed to establish the temporal stability of OCD symptom dimensions and the impact of additional variables on their stability in a large sample of children and adolescents diagnosed with OCD in a naturalistic setting.

2.1.2. Summary of the methods

The sample consisted of 74 participants meeting criteria for OCD referred to the National and Specialist Clinic for Children and Adolescents with OCD and Related Disorders at the Maudsley Hospital, London, United Kingdom. The mean age of the participants at baseline was 13.5 years (standard deviation [sd] = 2.6; range = 8 – 18). Fifty of those were males (67.7%). At baseline, participants were assessed with the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) and its ancillary Symptom Checklist (CY-BOCS-SC). CY-BOCS scores were in the range of moderate OCD (mean = 22.5, sd = 6.1; range = 11 – 40). The sample was re-assessed years later, being the mean length of follow-up 4.8 years (sd = 2.8; range = 1 – 11). Analysis of variance and multiple regression models were used to examine changes within and between symptom categories and the major symptom dimensions (*Cleaning*, *Forbidden thoughts*, *Hoarding*, and *Symmetry*) between the two assessment time points.

2.1.3. Summary of the results

Hypothesis 1: In general, symptom categories and symptom dimensions would show temporal stability over time similar to that observed in adult samples.

Changes within individual symptom categories of obsessions and compulsions were observed in approximately 15% – 45% of the cases. Although the majority of changes were from present at baseline to absent at follow-up, in some participants the direction of the change was the opposite.

Changes within symptom dimensions between baseline and follow-up were only significant for the *Cleaning* dimension (symptom improvement).

Additional exploratory analyses were conducted to assess whether age of participants at baseline, age of illness onset, illness duration, global OCD symptom severity at baseline, and length of follow-up were significant predictors of the percentage of change over time within each dimension. Non-significant results suggested that none of these variables had an effect on the temporal stability of the symptom dimensions.

Hypothesis 2: Symptom dimensions would remain stable when controlling for treatment effects (as changes in symptom dimensions could be confounded with overall reduction in OCD severity attributable to the intervention).

When excluding participants whose OCD had remitted at follow-up (n = 42) from the analyses, the previously observed differences in symptom categories and symptom dimensions (see *Hypothesis 1* above) were no longer significant.

Hypothesis 3: Endorsing a symptom dimension at baseline would be the strongest predictor of endorsing that corresponding dimension at follow-up.

Multiple regression analyses showed that for each symptom dimension at follow-up, the only significant predictor was the same dimension at baseline. The only exception was that the *Symmetry* dimension at baseline, which was additionally predictive of *Hoarding* symptoms at follow-up. The magnitude of the partial correlation coefficients was moderate, ranging from .25 to .35. These magnitudes improved only marginally when excluding the 42 individuals who no longer met criteria for OCD at follow-up (partial correlations range = .22 – .44).

2.1.4. Main conclusions

Confirming similar work in adults with OCD, the results showed that the content of OCD symptoms in young people is relatively stable across time. Most changes were attributable to clinical improvement/remission and occurred within rather than between symptom dimensions.

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Are the symptoms of obsessive-compulsive disorder temporally stable in children/adolescents? A prospective naturalistic study

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ABSTRACT

Obsessive-compulsive disorder (OCD) symptoms tend to be temporally stable in adults, but much less is known about their stability in young people. We examined the temporal stability of OCD symptoms in a clinical pediatric sample. As part of a naturalistic longitudinal study, 74 children and adolescents with OCD were assessed with the Children's Yale-Brown Obsessive Compulsive Scale on two separate occasions ranging from 1 to 11 years apart (average 5 years). Analysis of variance and multiple regression models examined changes within and between symptoms and symptom dimensions. Changes within individual symptom categories were observed in approximately 15–45% of the cases, depending on the specific symptom. In most of those cases, symptoms went from present to absent at follow-up rather than from absent to present. Changes were no longer significant when individuals who were in remission at follow-up were excluded. Multiple regression analyses indicated that the strongest predictor of a particular symptom dimension at follow-up was the presence of the same dimension at baseline. Shifts from one dimension to another were rare. The content of OCD symptoms is relatively stable across time in young people. Most changes observed were attributable to clinical improvement/remission and occurred within rather than between symptom dimensions.

1. Introduction

Obsessive-compulsive disorder (OCD) can be a chronic and persistent disorder that is relatively prevalent both in children and adults and is associated with high comorbidity and reduced quality of life (Heyman et al., 2001; Kessler et al., 2005; Storch et al., 2012). The symptoms of OCD are clinically heterogeneous (Leckman et al., 2009; Mataix-Cols et al., 2005). This phenotypic heterogeneity is thought to reflect etiological heterogeneity, as there are shared genetic and environmental risk factors that may be common to all OCD symptom dimensions, but also some of which might be dimension-specific (Grisham et al., 2011; Iervolino et al., 2011; Taylor et al., 2010). At least four relatively independent symptom dimensions have been identified and widely replicated: (a) Cleaning, (b) Forbidden thoughts, (c) Symmetry, and (d) Hoarding (Bloch et al., 2008). These symptom dimensions appear to be invariant across different cultures and age groups (Bloch et al., 2008). Factor analytical studies of OCD symptoms in children, adolescents, and adults have also revealed highly consistent symptom structures, suggesting that the fundamental architecture of OCD symptoms remains consistent throughout the lifespan (Mataix-Cols et al., 2008; Stewart et al., 2008).

In adults, despite the common clinical perception that the content of OCD symptoms frequently changes over time, the available evidence from longitudinal studies does not support this. Indeed, a series of well conducted studies, using both clinical and epidemiological samples, have converged to support the conclusion that the content of OCD symptoms is remarkably stable over time, with some symptoms waxing and waning *within* symptom dimensions but rarely involving shifts *between* dimensions (Fullana et al., 2009, 2007; Mataix-Cols et al., 2002; Rufer et al., 2005). However, prospective longitudinal investigations of the temporal stability of OCD symptoms in children and adolescents are rare, particularly during the crucial transition from adolescence to young adulthood. In one such study, Rettew et al. (1992) found that in a sample of 79 children and adolescents with OCD, no patient maintained the same constellation of symptoms from baseline to follow-up carried out 4 years later

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on average. However, the authors acknowledged that "many patients dramatically changed their ritualistic behavior without changing [symptom] categories" (p. 1054). More recently, Delorme et al. (2006) studied a group of pediatric patients (N=42) who were followed-up for a mean length of 3.8 years and concluded that most of the symptom dimensions were unchanged across time. In agreement with the adult studies that employed a similar methodology, Delorme et al. (2006) found that symptom dimensions remained essentially unmodified and shifts from one dimension to another were rare.

The symptom presentation of OCD in young people may depend on their developmental stage, and a number of developmental factors may play a role in the apparent (in)stability of symptoms across the developmental period. For example, in cross-sectional research, Geller et al. (2001) found that, compared to adults, children and adolescents with OCD had a higher prevalence of obsessive fears of loss or harm to loved ones or self, as well as increased prevalence of hoarding/saving compulsions. In the same study, adolescents had a higher prevalence of sexual obsessions compared to both children and adults. Furthermore, the diagnostic boundaries of OCD may not always be easy to establish, as a significant proportion of childhood-onset OCD cases ascertained at one point will be sub-threshold at a later time point and vice versa (Berg et al., 1989; Peterson et al., 2001; Zohar and Felz, 2001). Some ritualistic behaviors are normative in early childhood (Leckman and Bloch, 2008). Different types of normal ritualistic behavior emerge at different developmental ages; for example, a need to arrange things 'just right' or in a symmetrical pattern appears first, followed by the child's being concerned with dirt and germs, and finally, the urge to collect and store objects (Evans et al., 1997; Zohar and Felz, 2001). The diagnosis of OCD usually involves additional criteria including psychological resistance, a sense of subjective distress, and egodystonia, all of which require a certain degree of self-understanding, self-perception, and abstract thinking that may not be achieved until a given period in the cognitive development of the child (Evans and Leckman, 2006).

The aim of this prospective naturalistic study was to establish the temporal stability of OCD symptom dimensions in a pediatric sample of patients with OCD, over an average follow-up period of 5 years. Based on the adult literature, it was predicted that symptom dimensions of OCD would be largely stable over time and that shifts from one symptom dimension to another would be rare. The impact of additional variables on the stability of the symptom dimensions, such as age of the participant, illness duration at baseline, length of follow-up, and remission status at follow-up was also examined.

2. Methods

2.1. Participants

The sample consisted of 74 children and adolescents who received a diagnosis of OCD at the National and Specialist OCD Clinic for Young People at the Maudsley Hospital (London, UK) between July 1996 and June 2005. The clinic provides specialist assessment and treatment for young people with OCD (Nakatani et al., 2009). Treatment consists of protocol-driven cognitive-behavioral therapy largely focused on exposure with response prevention (March and Mulle, 1998), with or without medication, according to the NICE guidelines (National Collaborating Centre for Mental Health, 2006). These participants were part of a larger naturalistic follow-up study, reported in detail elsewhere (Micali et al., 2010, 2011). Of the 142 children and adolescents who were eligible and accepted participation in the larger study, 74 had complete baseline and follow-up data regarding symptom dimensions, measured with the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS), and were included in the present investigation. There were no significant differences on any baseline characteristics between these 74 participants and the remaining patients who were not included in this analysis (all $p > 0.05$, data available upon request).

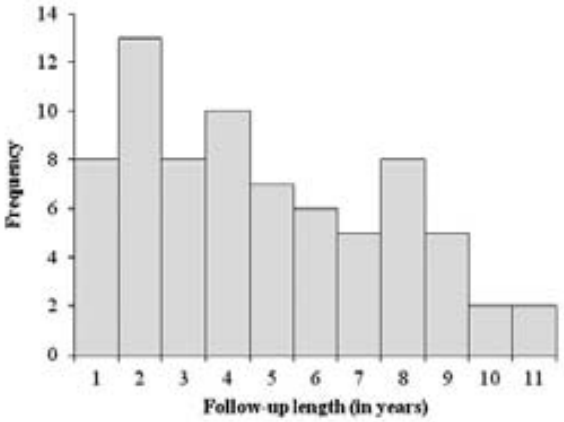

Fig. 1. Frequency distribution of the length of follow-up (in years) of the 74 pediatric patients with OCD included in the analysis.

Fifty (67.6%) were boys and 24 (32.4%) were girls. The mean age of the participants at baseline was 13.5 years (S.D.=2.6; range 8–18). When first assessed in the clinic, families were asked about onset of impairing OCD symptoms, to give an estimate of duration of illness, revealing a mean duration of 4.1 years (S.D.=3.1; range 0–13). The mean length of the follow-up period was 4.8 years (S.D.=2.8; range 1–11; median=4.1; see Fig. 1). The mean age of the participants at follow-up was 18.3 years (S.D.=3.6; range 12–28). Forty-two (56.8%) of the 74 patients no longer met criteria for OCD at follow-up and were considered to be in remission.

The study received ethical approval from the South London and Maudsley NHS Foundation Trust and the Institute of Psychiatry Research Ethics Committees.

2.2. Measures

An initial clinical assessment was completed by experienced clinicians specializing in the diagnosis and management of OCD. ICD-10 criteria were used to make psychiatric diagnoses (for details, see Micali et al., 2010). The CY-BOCS (Scahill et al., 1997; Storch et al., 2006) and its accompanying symptom checklist (CY-BOCS-SC), a list of more than 50 common obsessions and compulsions organized under 13 major symptom categories plus two categories of miscellaneous obsessions and compulsions, were carefully administered by trained clinical psychologists on the day of the initial assessment at the clinic.

At follow-up, the self-report versions of the CY-BOCS and the CY-BOCS-SC (Storch et al., 2006) were mailed to the participants who completed and posted them back to the research team. Additionally, all participants and their parents completed the computerized version of the Developmental and Well-Being Assessment (DAWBA) (Goodman et al., 2000) to establish the presence/absence of ICD-10 Axis I diagnoses at that point in time. The DAWBA is a well validated interview (face-to-face or web based) for parents and young people, resulting in ICD-10 and DSM-IV diagnoses algorithmically generated, which are then cross-validated by trained clinicians after review of the responses. In this study, anonymized computer ratings were reviewed by a clinically trained rater (NM) to generate final ICD-10 diagnoses at follow-up (for details, see Micali et al., 2010, 2011).

2.3. Data analyses

If a patient endorsed any of the individual symptoms under each of the 13 major symptom categories of the CY-BOCS-SC, a score of one was given (present). If none of the individual items were endorsed, that particular category was scored zero (absent). For each of the 13 symptom categories, McNemar's tests were used to determine the likelihood of changes in symptoms at follow-up compared to baseline.

Following the methodology described by Leckman et al. (1997) and subsequently used by others (e.g., Mataix-Cols et al., 2008), the number of currently endorsed symptoms under each of the 13 major symptom categories of the CY-BOCS-SC was summed in order to take full advantage of the variance within the data. This method offers an approximation of the severity of each symptom type. Next, an algorithm based on the meta-analysis by Bloch et al. (2008) was applied. Briefly, the scores of the contamination obsessions and cleaning compulsions were summed to form the 'Cleaning' dimension. The scores of the aggressive, sexual, religious, and somatic obsessions as well as checking compulsions were summed to form the 'Forbidden thoughts' dimension. Symmetry obsessions and ordering/arranging, counting, and repeating compulsions were summed to form the 'Symmetry' dimension. Finally, hoarding obsessions and compulsions were

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summed to form the 'Hoarding' symptom dimension. The scores on the resulting four dimensions were used as independent variables in all subsequent analyses.

Because different categories of the CY-BOCS-SC and resulting symptom dimensions have unequal numbers of items/categories, we also re-coded the data as the mean number of items/categories endorsed within each category/dimension, rather than the sum. The results were nearly identical to those using the approach described above and will not be reported, but are available from the authors upon request.

Quantitative changes within each of the above OCD symptom dimensions from baseline to follow-up were analyzed using Wilcoxon tests. A series of stepwise multiple regression models were applied to assess potential changes between symptom dimensions across time. In these models, all four baseline symptom dimension scores were entered as independent variables and in turn each dimension score at follow-up was the dependent variable, as described by Mataix-Cols et al. (2002).

Significance level was set at $p < 0.01$ to control for possible type I errors due to multiple testing although levels at $p < 0.05$ were also reported as non-significant trends. Data were analyzed using SPSS version 15.0.

3. Results

3.1. Changes within individual categories of obsessions and compulsions

Frequencies for each of the 13 major symptom categories of the CY-BOCS at baseline and follow-up are shown in Table 1. For most symptom categories, approximately 60% of the participants maintained their symptoms between baseline and follow-up. McNemar's tests showed statistically significant changes ($p < 0.01$) from baseline to follow-up for aggressive obsessions and for cleaning compulsions. There were non-significant trends for checking, repeating, and ordering compulsions ($p < 0.05$). Although the majority of changes were from present at baseline to absent at follow-up, in some participants the direction of the change was from absent to present.

When those participants whose OCD had remitted at follow-up ($N = 42$) were excluded from the analyses, no significant changes were found on any symptom category between baseline and follow-up, with the exception of magical thinking obsessions, which showed a trend towards significance ($p = 0.039$).

Table 1
Changes within individual categories of obsessions and compulsions ($N = 74$).

Symptom category in CY-BOCS	Symptom present at baseline		Symptom present at follow-up		Changes from present to absent		Changes from absent to present		Total of patients whose symptoms changed	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%
Obsessions										
Contamination	52	70.3	49	66.2	13	17.57	10	13.51	23	31.08
Aggressive	59	79.7	35	47.3	29	39.19	5	6.76	34	45.95**
Sexual	17	23.0	16	21.6	6	8.11	5	6.76	11	14.86
Hoarding	22	29.7	19	25.7	12	16.22	9	12.16	21	28.38
Religious	24	32.4	19	25.7	14	18.92	9	12.16	23	31.08
Somatic	32	43.2	31	41.9	14	18.92	13	17.57	27	36.49
Magical Thinking	29	39.2	34	45.9	9	12.16	14	18.92	23	31.08
Compulsions										
Cleaning	51	68.9	33	44.6	26	35.13	8	10.81	34	45.95**
Checking	57	77.0	45	60.8	21	28.38	9	12.16	30	40.54*
Repeating	51	68.9	37	50.0	24	32.43	10	13.51	34	45.95*
Counting	32	43.2	27	36.5	17	22.97	12	16.22	29	39.19
Ordering	40	54.1	27	36.5	24	32.43	11	14.86	35	47.30**
Hoarding	27	36.5	18	24.3	18	24.32	9	12.16	27	36.49

* Significant change in symptoms, McNemar's test at $p < 0.05$.
** Significant change in symptoms, McNemar's test at $p < 0.01$.

3.2. Changes within symptom dimensions

Wilcoxon repeated measures tests showed significant differences over time ($p = 0.001$) on the Cleaning dimension, indicating a decrease of symptoms across time within this dimension. Changes on the Forbidden thoughts, Hoarding, and Symmetry dimensions were not significant (Fig. 2). Again, when patients who were in remission at follow-up were excluded from the analyses, changes from baseline to follow-up on the Cleaning dimension were no longer significant ($z = -0.40$, $p = 0.69$). In this case, only the Symmetry dimension showed a trend towards significance ($z = -2.40$, $p = 0.02$).

3.3. Other potential variables influencing symptom change

Additional exploratory multiple regression analyses were conducted to assess whether the age of participants at baseline, the age of illness onset, the illness duration, the global symptom severity at baseline (C-YBOCS total scores), and the length of follow-up were significant predictors of the percentage of change over time within each dimension. None of the regression models showed significant results (all $p > 0.05$; data available upon request), suggesting that these variables did not exert any effect on the temporal stability of the symptom dimensions.

3.4. Changes between symptom dimensions

Multiple regression analyses were employed to examine the extent to which changes from one dimension to another dimension occurred over time (i.e., *between* dimension changes). The results revealed that for each symptom dimension at follow-up, the only significant predictor was the same dimension at baseline (Table 2). The only exception was that the Symmetry dimension at baseline was additionally predictive of Hoarding symptoms at follow-up. However, the magnitude of the partial correlation coefficients was moderate, ranging between 0.25 for the Cleaning dimension and 0.35 for the Hoarding dimension. The magnitude of these correlations was only marginally improved by the exclusion of the 42 individuals who no longer met criteria for OCD at follow-up, ranging between 0.22 for the Forbidden thoughts dimension and 0.44 for the Symmetry dimension.

4. Discussion

This study examined the temporal stability of OCD symptoms in a pediatric sample of OCD patients who were re-examined on average 5 years after their initial assessment. This is the longest follow-up period studied to date exploring symptom dimensions

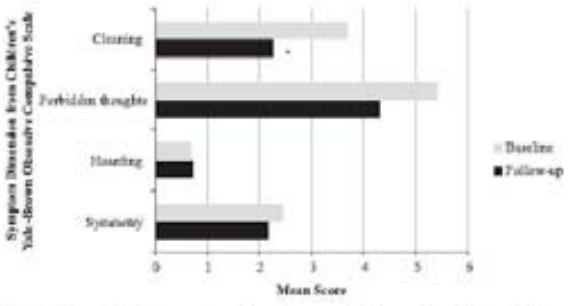

Fig. 2. Changes in OCD symptom dimension scores between baseline and follow-up (mean 4.8 years apart) among 74 youth with OCD. *Significant change over time on Wilcoxon repeated measures test ($z = -3.226$, $p = 0.001$).

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Table 2
Significant partial correlations between OCD symptom dimensions at baseline and follow-up, determined by multiple regression analyses ($N=74$).

	OCD dimensions at follow-up			
	Cleaning	Forbidden thoughts	Hoarding	Symmetry
OCD dimensions at baseline				
Cleaning	0.25*	−0.10	0.00	−0.12
Forbidden thoughts	−0.00	0.33**	0.22	0.11
Hoarding	−0.00	−0.03	0.35**	−0.01
Symmetry	−0.07	0.00	0.31**	0.32**

* Significance level: $p < 0.05$.
** Significance level: $p < 0.01$.

in OCD. The relatively large sample and available diagnostic data at follow-up allowed us to examine the role of clinical remission on the stability of symptoms during the follow-up period. Many of the participants were adolescents at baseline, and thus the design allowed us to examine temporal changes occurring at a crucial developmental stage of transition between adolescence and early adulthood.

The main finding of this study was that the majority of participants (approximately 60%) maintained their symptoms between baseline and follow-up, demonstrating temporal stability of symptoms. There was some variability to this within particular symptom categories. Statistically significant changes were found for aggressive obsessions and for cleaning compulsions (and for checking, repeating, and ordering rituals at a trend level), and in the majority of cases symptoms went from present at baseline to absent at follow-up rather than from absent to present, suggesting that the emergence of new symptoms was less likely. When the individual symptom categories were grouped into the four previously identified OCD symptom dimensions (Cleaning, Forbidden thoughts, Hoarding, and Symmetry) all remained stable between the baseline and the follow-up, except for the Cleaning dimension. This is consistent with results from a previous pediatric study by Delorme et al. (2006), who found that the contamination/cleaning dimension decreased significantly at follow-up while the other dimensions remained unchanged.

Interestingly, when patients who were in remission at follow-up ($N=42$) were excluded from the analyses, no significant changes were seen on any of the individual symptom categories or the symptom dimensions. Together with the fact that the most observed changes were from present to absent, rather than the other way around, this suggests that the remission status explains most of these changes. As not all these patients were treated at our clinic, it is unclear to what extent these changes were due to treatment effects, spontaneous remission, or other life events during the follow-up period. Additional exploratory correlation analyses showed that variables such as the age of the participants and the length of the follow-up did not correlate with the changes found within each dimension, suggesting that these variables did not have an effect on the stability of the dimensions over the time.

As well as changes within symptom dimensions, it was of interest to examine qualitative changes *between* symptom dimensions. That is, shifts from one dimension to another over time. Multiple regression analyses showed that no shifts between dimensions occurred, and indeed, the best predictor of endorsing a particular symptom dimension at follow-up was having endorsed the same dimension at baseline. The only significant cross-dimensional correlation was found between the Symmetry dimension at baseline and the Hoarding dimension at follow-up, although this association was small in magnitude. Nevertheless, the finding may have some significance as the excessive accumulation of objects in OCD is often considered to be secondary to symmetry or not-just-right concerns (Pertusa et al., 2010, 2008). For example, in a case series examining OCD-related hoarding, Pertusa et al. (2010) found that obsessive-compulsive symptoms related to the Symmetry dimension (including incompleteness and not-just-right experiences) were particularly likely to be associated with hoarding problems. The authors suggested that hoarding symptoms may not constitute a truly independent symptom dimension of OCD, as they frequently appear to be secondary to other OCD symptom presentations. This contrasts with primary hoarding, which is now thought to be a separate diagnostic entity (Mataix-Cols et al., 2010).

Of interest, the partial correlation coefficients in the current study were somewhat weaker than those reported in the adult studies (Mataix-Cols et al., 2002; Rufer et al., 2005), but were more similar to the pediatric study by Delorme et al. (2006). This suggests that, despite the fact that the best predictor of a future symptom is having had the same symptom in the past, the predictive power of this association is stronger in adult than it is in pediatric samples. The reasons for this are unclear but it may be related to a number of factors, including measurement error (in this study, the CY-BOCS was clinician-administered at baseline but self-completed at follow-up), difficulties separating developmentally normal rituals and symptoms of OCD, as well as the above-mentioned role of clinical remission. Alternatively, it is possible that other developmental factors may partly explain these findings. For example, subjective distress and egodystonia require a certain degree of self-understanding and abstract thinking that may not be sufficiently developed at the time of the initial assessment and may develop over time or as part of the treatment process.

Overall, the results are remarkably consistent with previous longitudinal studies that have employed similar designs in adult clinical (Mataix-Cols et al., 2002; Rufer et al., 2005) and non-clinical samples (Fullana et al., 2009, 2007; Novara et al., 2011), as well as in a previous pediatric study (Delorme et al., 2006). Taken together, our results are consistent with the notion that the *severity* rather than the *content* of the symptoms fluctuates over time and this may determine which symptoms patients are more likely to report to clinicians during psychiatric assessments. This may give the impression of symptom change. This does not mean that the emergence of new symptoms is impossible, particularly early on in the course of the disorder. Exactly when OCD symptoms appear for the first time in very young children is not well understood, partially because of the overlap between developmentally-normal ritualistic behavior and OCD symptoms. It is possible, however, that normal ritualistic behavior and OCD symptoms may be etiologically linked (Bolton et al., 2009).

4.1. Theoretical implications

The results have important implications for current conceptualizations of OCD. Increasing evidence suggests that OCD is not only a clinically but also an etiologically heterogeneous disorder. While there are likely to be genetic and environmental risk factors common to all individuals with OCD, as well as to individuals with other mood and anxiety disorders, there is also evidence that dimension-specific etiological factors are at least as important (Iervolino et al., 2011; Taylor, 2011). Furthermore, these symptom dimensions are associated with distinct comorbidity patterns (Leckman et al., 2007), neural substrates (Mataix-Cols et al., 2004b; Ruck et al., 2012; van den Heuvel et al., 2009), and childhood risk factors (Grisham et al., 2011). The finding that the major symptoms of OCD are temporally stable further supports the notion of etiologically independent symptom dimensions that overlap in various degrees in any given patient (Mataix-Cols et al., 2005). This temporal stability may be at least

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partially explained by genetic factors, as indicated by longitudinal twin studies (van Grootheest et al., 2007a, 2007b). Therefore, there is considerable merit in pursuing this line of research, as a full understanding of OCD is unlikely to be achieved without taking this heterogeneity into account.

4.2. Clinical implications

There are a number of findings in this study that could usefully inform clinical practice. The knowledge that most patients' symptom content remains fairly stable over time can potentially aid relapse prevention strategies. Informing young people and their parents that, should a relapse occur, this is likely to be in the form of the same symptoms that had been present in the past, can aid families to identify the early signs of a potential relapse and act quickly and appropriately. Families should also be informed that other *de novo* symptoms might also appear, but that is far less likely. We would encourage clinicians to perform thorough assessments of both current and past symptoms at the point of the first assessment, as the results here suggest that patient concerns are unlikely to deviate much over the course of time. Even if a symptom is endorsed as present in the past, there is a fair chance that it may reappear at a latter point in time, giving the false impression of a 'new symptom'. It is more plausible that symptoms may be 'dormant' for periods of time and then be reactivated, consistent with the often used term 'waxing and waning'.

4.3. Limitations

The study has several limitations. First, the CY-BOCS-SC has a number of important psychometric shortcomings, as discussed elsewhere (e.g., Mataix-Cols et al., 2004a). Furthermore, different categories of the CY-BOCS-SC include different numbers of items and categories including a higher number of items may be more likely to appear to change over time. This is a particular problem for the Hoarding dimension, which only includes four items (two under obsessions and two under compulsions). However, it is reassuring that when we recoded our data as the mean number of items/categories endorsed within each category/dimension, rather than the sum, the results were nearly identical. Nevertheless, future studies addressing this research question should employ more psychometrically sound instruments, such as the Dimensional Y-BOCS (Rosario-Campos et al., 2006), that were not available at the time the baseline data were collected. Second, different versions of the CY-BOCS-SC were used at baseline (clinician-administered) and follow-up (self-administered). This may have introduced a source of bias in the data. However, the likely result may have been an under-, rather than over-estimation of the temporal stability of the symptoms, and the consistency of our results with those of previous studies suggests that this is minimal. Third, although the sample size is larger than that of previous studies assessing the stability of the symptom dimensions in OCD youth, it is still relatively modest.

4.4. Conclusion

Consistent with previous studies in adults and contrary to popular belief, the content of OCD symptoms in young people is relatively stable across time and spans well into early adulthood. Most changes that occur in symptoms do so *within* rather than *between* symptom dimensions and are largely attributable to clinical remission.

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2.2. STUDY 2: Sexual obsessions in children and adolescents with OCD

Fernández de la Cruz, L., Barrow, F., Bolhuis, K., Krebs, G., Nakatani, E., Heyman, I., & Mataix-Cols, D. (2013). **Sexual obsessions in pediatric obsessive-compulsive disorder: Clinical characteristics and treatment outcomes.** *Depress Anxiety*, in press. DOI: 10.1002/da.22097.

2.2.1. Background

Sexual obsessions are a common presentation of OCD. They may include unwanted sexual thoughts about having sex with family members or children, fears about engaging in sexually aggressive behavior, or concerns about sexual orientation. In adult samples with OCD, sexual obsessions have been found to be more frequent in men, accompanied by other symptoms from the *Forbidden thoughts* dimension, and related to more distress and interference and an earlier age of OCD onset. Mixed results have been found regarding treatment response, with some reports suggesting that individuals with sexual obsessions respond poorer than individuals with symptoms from other symptom categories. In children, sexual obsessions have been largely disregarded. However, the fact that these symptoms may be alarming, misinterpreted as indicating risk to others, or confused with normal sexual development highlights the importance of studying this issue in a pediatric population. In this study we aimed to examine the demographic and clinical characteristics of sexual obsessions in a large sample of young people. Furthermore, we wanted to examine the treatment outcomes of OCD patients suffering from sexual obsessions compared with those OCD patients without.

2.2.2. Summary of the methods

The sample comprised 383 participants meeting criteria for OCD referred to National and Specialist Clinic for Children and Adolescents with OCD and Related Disorders at the Maudsley Hospital, London, United Kingdom. Mean age of the participants was 14.34 years (sd = 2.24; range = 7 – 18). Two hundred and sixteen were boys (56.4%). Participants were assessed at the time of the initial clinical assessment and, for those treated at the clinic (153 participants; 39.9%), again after treatment. For this latter group, treatment consisted of CBT involving ERP (with or without medication). The measures included the CY-BOCS (mean total score at intake = 26.32, sd = 5.65) and its accompanying Symptom Checklist (CY-BOCS-SC), as well as the Children's Obsessive-Compulsive Inventory (ChOCI), the Family Accommodation Scale (FAS), the Strengths and Difficulties Questionnaire (SDQ), the Beck Depression Inventory for Youth (BDI-Y), and the Children's Global Assessment Scale (CGAS). Patients with and without sexual obsessions were compared on socio-demographic and clinical characteristics. Mixed-model analyses of variance compared treatment outcomes between groups.

2.2.3. Summary of the results

Hypothesis 1: Sexual obsessions would be a common symptom in the sample, and would be more prevalent in adolescents than in younger children.

According to the CY-BOCS-SC, 102 patients (26.6%) presented with sexual obsessions at the initial assessment. In this group, the most frequent sexual obsessions were forbidden or perverse sexual thoughts, images, or impulses (n = 71, 74.7%).

Participants with sexual obsessions were slightly, albeit significantly, older than those without sexual obsessions (14.8 vs. 14.2; p = .006). As anticipated, sexual obsessions were more frequent in adolescents (around age 15 and older). However, sexual obsessions were found to be present across all ages (range = 8 – 17).

Hypothesis 2: Patients with sexual obsessions would also present with other symptoms from the same dimension (aggressive and religious thoughts). Also, individuals with sexual obsessions would be more depressed than their counterparts who do not endorse sexual obsessions.

As expected, the group with sexual obsessions reported having significantly more frequent aggressive and religious obsessions. Also, they reported more magical thinking and the fear of saying certain things from the miscellaneous category, and more superstitious games and several other compulsions from the miscellaneous category (i.e., mental rituals; need to tell, ask, or confess; and blinking or staring) than their counterparts without sexual obsessions.

Participants with sexual obsessions did show significantly higher depression levels and, also, were found to score marginally higher in OCD symptom severity, as assessed by the CY-BOCS.

Hypothesis 3: The presence of sexual obsessions would not be associated with poorer treatment outcome, as long as treatment is delivered by a specialist team and adapted to the developmental needs of the child.

Mixed-model ANOVA analyses did not find differential treatment outcome in those with sexual obsessions (n = 50) vs. those without (n = 103). The results were independent of whether the patients were on medication or not.

2.2.4. Main conclusions

Sexual obsessions are common in pediatric OCD and, although they may be associated with particular clinical features (i.e., higher scores in depression and slightly more severe OCD), they do not interfere with treatment response. We also concluded that these symptoms are benign and should not be misinterpreted as posing a risk to others.

Research Article

SEXUAL OBSESSIONS IN PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER: CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES

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Background: *Sexual obsessions are common in adults with obsessive-compulsive disorder (OCD), cause great distress, and are sometimes misinterpreted as indicating risk to others. Little is known about the prevalence, clinical correlates, and prognosis of such symptoms in young people.* **Methods:** *Three hundred and eighty-three patients referred to a specialist pediatric OCD clinic were administered a series of measures at intake and, for those treated at the clinic, again after treatment. Patients with and without sexual obsessions were compared on socio-demographic and clinical characteristics. Mixed model analyses of variance compared treatment outcomes in both groups.* **Results:** *A quarter of patients had sexual obsessions at baseline (age range 8–17); they had slightly more severe OCD symptoms and were more depressed than those without sexual obsessions. Aggressive and religious obsessions, magical thinking, fear of saying certain things, repeating rituals, superstitious games, mental rituals, and the need to tell, ask, or confess were more frequent in participants with sexual obsessions. Crucially, no differences in treatment outcome were found between the groups.* **Conclusions:** *Sexual obsessions are common in pediatric OCD, even in very young children. Although they may be associated with particular clinical features, they do not interfere with treatment response. The occurrence of sexual obsessions in children should be recognized and these symptoms understood as ordinary, nonthreatening OCD symptoms, which pose no risk to others. They respond to the standard treatment strategies, so children and families should receive the usual message of optimism regarding the chances of recovery. Depression and Anxiety 00:1–9, 2013.*

Key words: *adolescents; children; obsessive-compulsive disorder; risk; sexual obsessions*

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INTRODUCTION

Obsessive-compulsive disorder (OCD) is characterized by unwanted and intrusive thoughts and repetitive behaviors or rituals. Obsessions are highly heterogeneous in nature and may commonly involve "forbidden" thoughts, such as aggressive, religious, or sexual obsessions.[1,2] The latter may include unwanted thoughts about sexual acts with family members or young children, sexually aggressive behavior, unfaithfulness, and homosexual acts.[3,4] Sexual obsessions may remain undetected because sufferers are often embarrassed to disclose symptoms that might be perceived as unacceptable.[5] Despite this, they have been found to be common in adults with OCD, with reported prevalence ranging from 5–24%.[6,7] Sexual obsessions are also common in adolescent patients, with a lower prevalence reported in younger children.[8]

Sexual obsessions have been rarely studied in their own right, but appear to have specific clinical correlates. Adult patients with sexual obsessions are more likely to be male,[4,9,10] tend to experience other types of "forbidden" thoughts (e.g. aggressive, religious obsessions),[3] to suffer more distress and interference,[4,11] and to have an earlier age of OCD onset,[3] compared to patients without such symptoms. In a large multicentric study, the presence of sexual/religious symptoms was strongly associated with suicidal thoughts and plans.[12]

Much less is known about sexual obsessions in pediatric samples. There are at least two reasons why it is important to further study these obsessions, particularly in young people with OCD. First, there is some indication that sexual obsessions and other "forbidden" thoughts may be associated with poorer response to cognitive-behavior therapy (CBT)[13–16] and serotonin reuptake inhibitors (SRIs).[13,17] However, other studies have not found such an association.[18–22] Second, sexual obsessions tend to cause alarm among family members and professionals, often being misinterpreted as indicating risk. For example, thoughts of sexual acts with young children may erroneously be understood as indicating emerging pedophilia, without proper consideration being given to the possibility of OCD. Sufferers may be subjected to lengthy or inappropriate risk assessments motivated by the improbable case that they could act on their intrusive thoughts,[23] which is in turn likely to fuel the individuals own fear that they are dangerous. Two such examples from our clinic are presented in Table 1.

Similarly, it is not uncommon for clinicians to assume that a young person with intrusive sexual thoughts has been abused, leading to excessive questioning, investigations, or examination, that can do significant harm.[23] Healy et al.[24] described two cases of pediatric OCD where child sexual abuse was suspected due to the sexual nature of the symptoms. However, in both cases it was considered unlikely after clinical assessment. Nonetheless, in another case series, Freeman and Leonard[25] reported onset of OCD in two young children after sexual abuse or sex play, and suggested that these experiences had become incorporated into the obsessional content. Therefore, it is appropriate to consider sexual abuse when assessing sexual obsessions while remaining aware that excessive questioning may be harmful.[23]

Obsessions relating to sexual orientation and sexual identity can also potentially lead to misinterpretation and delayed treatment, particularly in the peripubertal period. Such obsessions and the related distress may be misunderstood as being the result of a sexual identity conflicts and prevent access to evidence-based treatment for OCD.[4] For example, Williams[26] described a young man with obsessions about sexual orientation where the therapist failed to recognize the sexual thoughts as symptom of the OCD, resulting in an increase of symptoms and suicidal ideation. As another example of confusion surrounding this issue, in response to a patient complaint, the Swedish Ombudsman against discrimination on grounds of sexual orientation determined that the Yale-Brown Obsessive Compulsive Scale Symptom Checklist (Y-BOCS-SC) item assessing homosexual thoughts is discriminatory and should be removed because there is no corresponding "heterosexual thoughts" item.[27] Clearly, the Ombudsman failed to appreciate the distinction between sexual orientation and unwanted thoughts relating to sexual orientation.[27]

Given the paucity of data on sexual obsessions in pediatric OCD, this study examined the demographic and clinical characteristics of pediatric OCD patients with sexual obsessions referred to a specialist clinic. In addition, we tested the hypothesis that the presence of sexual obsessions would be associated with poorer treatment outcome.

METHODS

PARTICIPANTS

Participants were 383 youth consecutively referred to the National and Specialist Pediatric OCD & Related Disorders Clinic at the Maudsley Hospital, London between 2004 and 2011 and meeting ICD-10[28] diagnostic criteria for OCD. A multidisciplinary clinical team specializing in the diagnosis and management of OCD conducted an initial comprehensive clinical assessment lasting approximately 3 hours. Detailed sociodemographic and clinical information was gathered from the patients and their parents and diagnoses of OCD and any other comorbid disorders were made according to ICD-10 criteria.

One hundred and fifty-three participants (39.9%) received treatment at the clinic. Patients are often referred to our clinic for a specialist assessment only and are then referred back to their local teams for treatment. There were no significant differences in any relevant demographic or clinical variables between those participants who were treated at the clinic and those who were not, including OCD severity (CY-BOCS Total score: 26.7 versus 26.0, respectively; Student's $t = -1.056$, $P = .291$), although the percentage of participants with sexual obsessions was significantly higher among those treated at the clinic (32.7% versus 22.6%; $\chi^2 = 4.769$, $P = .029$).

All data used in the current study were collected as part of clinical practice but are of high standard and routinely employed for research purposes [e.g. 29]. Approval for the study was received from the South London and Maudsley Clinical Audit and Effectiveness Committee.

TABLE 1. Two examples of sexual obsessions being misinterpreted as posing risk

Case 1.
Kevin was a 15-year-old boy who presented with moderate to severe OCD (CY-BOCS score = 26), despite being treated with sertraline 100 mg and 15 sessions of CBT. His most distressing obsessions were fears that he had sexually abused his younger cousin in the past, and worries that he may therefore be a pedophile and abuse other children in the future. Despite a diagnosis of OCD having been given and recognition that Kevin experienced the thoughts as abhorrent and performed compulsions in an attempt to neutralise them, a social services investigation was carried out to establish whether Kevin had indeed abused his cousin. Kevin's worries were found to be unsubstantiated. The process caused Kevin considerable distress resulting in depressive symptoms and suicidal ideation. It also fuelled his belief that his sexual thoughts were not part of OCD, causing reluctance to disclose symptoms to others and avoidable delays and difficulties in treatment. Kevin was referred to our specialist OCD clinic for further treatment. Following 14 sessions of CBT for OCD, Kevin was able to gain insight into his symptoms as being part of his OCD and achieved a remission of his OCD (posttreatment CY-BOCS score = 8).
Case 2.
Josie was a 15-year-old girl who presented with moderately severe OCD (CY-BOCS score = 24) and maladaptive coping strategies (e.g. self-harm, alcohol use). Josie's symptoms included aggressive homosexual and incestuous obsessions and concerns that she may act on unwanted impulses, leading to mental rituals and reassurance seeking. Josie reported having engaged in sexual play with girls of the same age at 6 and 8, and had stated that she enjoyed the experience. This led to concern among professionals that she may be sexually deviant and represent a risk to others, despite symptoms indicative of OCD (high level of distress when thoughts present, compulsive behaviors, obsessive doubting). Josie's symptoms were initially misdiagnosed as psychosis and treated with aripiprazole 15 mg. Due to the perceived risk to others, Josie had a brief psychiatric admission and was referred to social services. A referral to forensic services was also considered. However, following an assessment for and diagnosis of OCD, Josie was able to recognize her thoughts as intrusive and ego-dystonic. She engaged in eight sessions of CBT for OCD, in conjunction with fluoxetine 20 mg, and made significant gains including no longer experiencing any sexual obsessions (posttreatment CY-BOCS score = 8).

MEASURES

The Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) and its accompanying symptom checklist (CY-BOCS-SC) were administered to assess the severity and phenomenology of the OCD symptoms.[30,31] The Sexual Obsessions section of the CY-BOCS-SC comprises four different items that were individually recorded: "Forbidden or perverse sexual thoughts, images, impulses," "Content that involves homosexuality," "Sexual behavior towards others (aggressive)," and "Other." The CY-BOCS was readministered at the end of the CBT treatment sessions as the main measure of treatment outcome.

The Children's Obsessive-Compulsive Inventory (ChOCI) is a self- and parent-report instrument developed to assess obsessive-compulsive symptoms and their impairment in young people. The ChOCI has shown good internal consistency and criterion validity.[32,33]

The Family Accommodation Scale (FAS)[34] assesses the degree to which family members have accommodated the child's OCD symptoms and the level of distress or impairment that the family members and patient experience as a result. The FAS has adequate internal consistency and good inter-rater reliability[35] and has been widely used in pediatric OCD studies [e.g.[36,37]].

The Beck Depression Inventory for Youth (BDI-Y) is a widely used measure of depression, which has good internal consistency and test-criterion validity.[38]

The Strengths and Difficulties Questionnaire (SDQ) assesses psychological adjustment of children and adolescents. Many studies from diverse countries have supported its validity and clinical utility.[39]

TREATMENT

All children treated at the clinic ($N = 153$) received CBT from experienced therapists or trainees under close supervision. CBT was protocol-driven and largely focused on exposure with response prevention (ERP), with parental involvement. It involved the following key components: psychoeducation about OCD and anxiety; development of an exposure and response prevention hierarchy; graded exposure with response prevention; and relapse prevention. In most cases, 12–14 sessions were offered. Typically, sessions were weekly and 1-hour long. Patients with and without sexual obsessions received an equivalent number of CBT sessions (13.9 versus 13.8 sessions, respectively; Student's $t = -.023$, $P = .982$).

Fifty-two of the participants with posttreatment data (34%) received medication for OCD (SRIs) in addition to CBT. Of those, 12 were also on low doses of antipsychotics (mostly risperidone) as an augmentation strategy. In most cases, medication was started and had reached a stable dose before CBT commenced. Those who received medication along with CBT were found to be slightly older (14.9 versus 13.9 years; Student's $t = -2.610$, $P = .010$) and had more severe OCD (29.5 versus 25.1 on the CY-BOCS total score; Student's $t = -4.629$, $P < .001$). Finally, the medication group had a higher proportion of participants with sexual obsessions (44.2% versus 26.7%; $\chi^2 = 4.777$, $P = .029$).

STATISTICAL ANALYSES

Data were analyzed using SPSS version 15.0 for Windows. Between-group differences were tested using either Chi-square tests for categorical data, Mann–Whitney U tests for ordinal data, or Student's t tests for continuous independent data. A mixed model ANOVA was used to test for a differential effect of group (sexual obsessions/no sexual obsessions) on responsiveness to treatment. All statistical tests were two-tailed. Significance level was set at $P < .05$. Sample sizes may vary for some of the analyses as a result of missing data.

RESULTS

SAMPLE CHARACTERISTICS

Two hundred and sixteen (56.4%) participants were boys. The mean age of the participants at baseline was 14.3 years ($SD = 2.2$; range = 7–18) and the mean age at onset of their OCD was 10.7 years ($SD = 3.1$, range = 3–18). The mean total CY-BOCS score was 26.3 ($SD = 5.6$), indicating moderately severe symptoms. According

TABLE 2. Demographic and clinical characteristics of pediatric OCD patients with and without sexual obsessions ($N = 383$)

	Participants with sexual obsessions ($N = 102$, 26.6%)		Participants without sexual obsessions ($N = 281$, 73.4%)		Statistic	
DEMOGRAPHICS	*N*	%	*N*	%	Chi-square	*P*
Boys	60	58.8	156	55.5	.333	.564
On medication for OCD	47	46.1	99	35.2	3.733	.053
Any comorbid disorder	30	29.7	80	29.0	.018	.892
	Mean	*SD*	Mean	*SD*	Student's *t*	*P*
Age at assessment	14.8	2.0	14.2	2.3	−2.796	.006
Age of OCD onset	11.0	3.2	10.6	3.1	−1.282	.201
OCD MEASURES	Mean	*SD*	Mean	*SD*	Student's *t*	*P*
CY-BOCS						
CY-BOCS Obsessions	13.7	3.0	12.5	3.0	−3.395	.001
CY-BOCS Compulsions	13.7	2.9	13.4	3.0	−.904	.367
CY-BOCS total	27.4	5.6	25.9	5.6	−2.274	.024
ChOCI self-reported						
ChOCI obsessions	14.5	4.4	14.2	5.3	−.454	.650
ChOCI compulsions	14.9	4.3	15.4	4.4	.899	.369
ChOCI total	29.1	8.2	29.7	8.8	.535	.593
ChOCI parent report						
ChOCI obsessions	16.8	4.3	15.3	5.9	−2.313	.022
ChOCI compulsions	16.8	4.2	16.4	4.6	−.678	.498
ChOCI total	32.5	9.0	31.4	9.7	−.876	.382
FAS						
FAS mother	23.3	14.1	26.1	13.9	1.373	.171
FAS father	19.6	13.6	20.9	14.3	.561	.576
OTHER CLINICAL MEASURES	Mean	*SD*	Mean	*SD*	Student's *t*	*P*
BDI-Y (*T* score)	62.6	10.8	59.4	13.1	−2.269	.024
SDQ child, total score	20.6	5.3	19.5	4.7	−1.442	.151
SDQ parent, total score	19.7	4.7	19.3	5.1	−.484	.629

to the CY-BOCS-SC, 102 patients (26.6%) had current sexual obsessions at the initial assessment.

CONTENT OF SEXUAL OBSESSIONS

Data about the individual sexual obsessions items on the CY-BOCS-SC was available for 95 of the 102 participants in the sexual obsessions group. The most frequent sexual obsessions were forbidden or perverse sexual thoughts, images, or impulses ($n = 71$, 74.7%). Examples of these obsessions in our sample included worrying about being a pedophile or having thoughts about having sex with younger children, images of themselves having sex with family members, and images of having sex with dead people. Thoughts about aggressive sexual behavior toward others ($n = 39$, 41%), thoughts with content involving homosexuality ($n = 31$, 32.6%), and the category "other" ($n = 21$, 22.1%) were also frequent. Examples from the "other" category included worrying about making women pregnant after masturbating and worries that a boyfriend had been unfaithful.

COMPARISON OF PATIENTS WITH AND WITHOUT SEXUAL OBSESSIONS

There were no differences in terms of sex, age at onset of OCD, or presence of comorbid disorders (Table 2). Participants with sexual obsessions were slightly, but significantly, older than those without sexual obsessions (14.8 versus 14.2; Student's $t = -2.796$, $P = .006$). A detailed examination of the frequency of sexual obsessions by age showed that, although sexual obsessions were present across all ages (range 8–17), there was an abrupt increase of these symptoms taking place at around age 15 (Figure 1). More patients with sexual obsessions tended to be on medication for their OCD (SRIs) compared to patients without sexual obsessions (nonsignificant trend, $P = .053$) but a logistic regression model indicated that this was entirely explained by the older age of the medicated participants.

Participants with sexual obsessions scored marginally but significantly higher on the obsessions ($P = .001$) and total scores ($P = .024$) of the CY-BOCS and the obsessions subscale of the ChOCI (parent version, $P = .022$), compared to participants without sexual

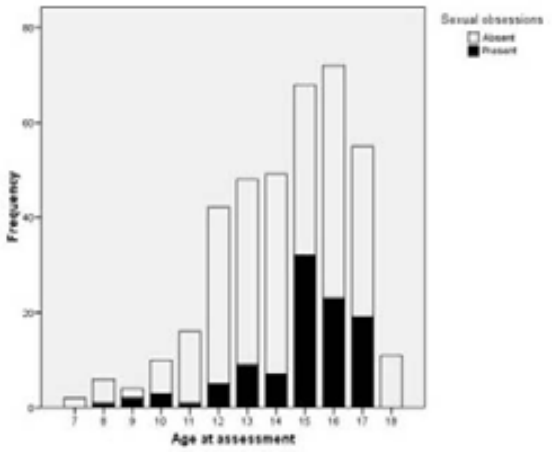

Figure 1. Frequency of participants with and without sexual obsessions by age.

obsessions. There were no between-group differences on the compulsions subscale of the CY-BOCS, the self-reported version of the ChOCI, or the family accommodation scores on the FAS (Table 2).

As shown in Table 3, aggressive and religious obsessions, magical thinking, the fear of saying certain things, superstitious games, mental rituals, the need to tell, ask, or confess, blinking or staring, and other rituals from the miscellaneous group were significantly more frequent in the group with sexual obsessions (all $P \leq .05$).

Both groups had equivalent scores on the SDQ (child and parent versions). Only the BDI-Y showed differences between the two groups, with a significantly higher *T* score, indicating more severe depressive symptoms in the sexual obsessions group ($P = .024$) (Table 2). There were no statistically significant between-group differences on the suicidal ideation item of the BDI-Y (item 4: *"I wish I were dead"*) (Mann–Whitney's $U = 10453.50$, $P = .221$).

TREATMENT OUTCOME

One hundred and fifty-three patients ($N = 50$ with sexual obsessions; $N = 103$ without) received CBT at the clinic. Mean pre- and posttreatment CY-BOCS scores for both groups are shown in Table 4. A mixed-model ANOVA with time as the within-subjects factor (pre- versus posttreatment) and group (with versus without sexual obsessions) as the between-subjects factor revealed a main effect of time [$F(1, 151) = 362.114$, $P < .001$], indicating a significant reduction in CY-BOCS total score over the course of the treatment. There were no significant main group [$F(1, 151) = 1.762$, $P = .186$] or time by group interaction [$F(1, 151) = .123$, $P = .727$] effects, indicating that the two groups improved similarly with treatment. A similar pattern of results emerged when the obsessions and compulsions subscales of the CY-BOCS were analyzed separately; there were main effects of time [$F(1, 150) = 352.922$, $P < .001$ and $F(1, 150) = 285.377$, $P < .001$, respectively] but no significant time by group interactions [$F(1, 150) = .226$, $P = .635$ and $F(1, 150) = .024$, $P = .878$, respectively]. However, while no main effects of group were found on the compulsions subscale [$F(1, 150) = .166$, $P = .684$], the obsessions subscale did show a significant group effect [$F(1, 150) = 4.566$, $P = .034$], attributable to the significantly higher CY-BOCS obsessions scores in the sexual obsessions group (see Table 4).

In order to investigate potential effects of medication, we next introduced medication status as an additional factor in the mixed-model ANOVA. The results indicated significant main effects of time [$F(1, 149) = 320.189$, $P < .001$] and medication [$F(1, 149) = 27.648$, $P < .001$], medicated patients being more severe at both time points, but no significant main group effect [$F(1, 149) = .250$, $P = .617$], and no significant time by group [$F(1, 149) = .603$, $P = .438$], time by medication [$F(1, 149) = 1.247$, $P = .266$], or time by group by medication [$F(1, 149) = .861$, $P = .355$] interactions. Equivalent results were obtained for the CY-BOCS obsessions and compulsions subscales (data available upon request).

DISCUSSION

To our knowledge, this is the first study specifically exploring sexual obsessions in a large sample of pediatric patients with OCD. These symptoms are not only common, with more than one in four young people with OCD reporting sexual obsessions, but they were also associated with marginally higher symptom severity and more severe levels of depression. The most frequent concerns involved forbidden or perverse sexual thoughts, images, or impulses, which were endorsed by over 70% of the young people who reported sexual obsessions. As in adult studies, sexual obsessions tended to appear alongside other "forbidden" thoughts such as aggressive and religious obsessions, magical thinking, fear of saying certain things, and associated rituals such as repeating rituals, superstitious games, mental rituals, and the need to tell, ask, or confess.[1,2]

Young people with sexual obsessions were marginally, yet significantly, older than those without sexual obsessions. Similarly, Geller et al.[8] reported a higher proportion of sexual obsessions in adolescents with OCD, compared to children and adults. In our sample, sexual obsessions were particularly common in children aged 15 or older. However, clinicians should be aware that sexual obsessions might be also present in much younger children (as young as eight in our sample). These results highlight the importance of openly and directly enquiring about sexual obsessions in the assessment process, even in very young children.

The association between sexual obsessions and depressive mood is in line with the trend found by Grant et al.[3] in an adult sample and also consistent with older literature suggesting that depressed mood is primarily related to obsessions, rather than compulsions, in

TABLE 3. Frequencies of obsessions and compulsions in pediatric OCD patients ($N = 383$) with and without sexual obsessions, according to the CY-BOCS-SC

	Participants with sexual obsessions ($N = 102$, 26.6%)		Participants without sexual obsessions ($N = 281$, 73.4%)		Statistic	
	N	%	*N*	%	Chi-square	*P*
Obsessions						
Contamination	73	73.7	199	71.6	.169	.681
Aggressive	84	84.8	199	71.6	6.864	.009
Hoarding	33	33.3	83	29.7	.441	.506
Magical thinking	44	44.4	91	32.6	4.453	.035
Somatic	36	36.4	86	30.8	1.026	.311
Religious	56	56.6	98	35.1	13.913	.000
Miscellaneous obsessions						
Need to know/remember	28	28.3	54	19.4	3.429	.064
Fear of saying certain things	21	21.2	33	11.8	5.255	.022
Fear of not saying the right thing	21	21.2	46	16.5	1.119	.290
Intrusive (nonviolent) images	9	9.1	14	5.0	2.121	.145
Intrusive sound, word, music, number	10	10.1	17	6.1	1.770	.183
Other	10	10.1	32	11.5	.139	.710
Compulsions						
Cleaning	78	78	202	72.9	.991	.320
Checking	82	82	203	73.6	2.857	.091
Repeating	68	68.7	161	58.1	3.418	.064
Counting	45	45	114	40.9	.518	.472
Ordering	44	44	143	51.4	1.429	.232
Hoarding	36	36	82	29.4	1.500	.221
Superstitious games	46	46	91	32.6	5.713	.017
Rituals involving others	74	74	181	65.1	2.649	.104
Miscellaneous compulsions						
Mental rituals	54	54	93	33.5	13.065	.000
Need to tell, ask, confess	40	40	59	21.2	13.414	.000
Measures to prevent harm	12	12	32	11.5	.017	.896
Ritualized eating	25	25	59	21.2	.607	.436
List making	11	11	33	11.9	.054	.816
Touch, tap, rub	44	44	105	37.8	1.195	.274
Just right	38	38	93	33.5	.671	.413
Blinking, staring	31	31	42	15.1	11.920	.001
Trichotillomania	6	6	7	2.5	2.685	.101
Self-harming	7	7	20	7.2	.004	.948
Other	17	17	24	8.6	5.381	.020

OCD.[40] Torres et al.[12] recently reported that adults with sexual/religious symptoms were more likely to have suicidal thoughts and behavior, a finding that we could not replicate, perhaps due to the single item nature of our assessment. In any case, monitoring of mood and suicidality may be particularly important in this group.

Contrary to some of the previous literature,[13–16] patients with sexual obsessions were just as likely to respond to developmentally tailored CBT as patients without such symptoms. This was true independently of whether the patients were on SRI medication or not, and taking into account that patients with sexual obsessions were slightly more likely to be on medication.

The reason why patients with sexual obsessions were more likely to receive treatment at our national and specialist OCD clinic (rather than being sent back to their local teams for treatment) is unclear, but is an interesting question in its own right. Patients with sexual obsessions were more severely impaired and more depressed, so it may be that clinicians felt that both CBT and medication were needed to achieve optimal response. To our knowledge, there is no strong evidence to suggest that patients with more severe obsessions (sexual or otherwise) are more likely to benefit from a combined treatment of CBT plus SRI versus CBT monotherapy, unless there is a clear clinical indication such as severe depression or suicidal risk. An alternative, perhaps not incompatible, explanation may be that patients, families, and professionals are more alarmed by such symptoms and therefore specialist treatment is seen as the safest, most assertive option. In any case, our results suggest that sexual obsessions are as responsive to CBT (with or without medication) as other types of symptoms.

TABLE 4. Mean CY-BOCS scores at pre- and posttreatment in pediatric OCD patients with and without sexual obsessions ($N = 153$)

	Participants with sexual obsessions ($N = 50$)		Participants without sexual obsessions ($N = 103$)		Statistic	
CY-BOCS scores	Mean	*SD*	Mean	*SD*	*t*-test	*P*
CY-BOCS obsessions						
Pretreatment	14.0	3.4	12.6	3.0	−2.463	.015
Posttreatment	7.7	4.3	6.7	4.1	−1.405	.162
CY-BOCS compulsions						
Pretreatment	13.7	3.5	13.4	3.2	−.486	.628
Posttreatment	7.5	4.2	7.4	4.2	−.230	.819
CY-BOCS total						
Pretreatment	27.7	6.6	26.1	5.7	−1.563	.120
Posttreatment	15.2	8.1	14.1	8.1	−.833	.406

As mentioned earlier, sexual obsessions can be alarming and distressing for both families and clinicians, as they may erroneously be perceived to indicate a potential risk. This may lead to unnecessary lengthy and damaging risk assessments, which may in turn provoke greater distress, rituals, avoidance, and mistrust of health professionals. This could be avoided if the classical psychopathology/phenomenology of OCD were better recognized, incorporated appropriately into the case formulation, symptoms normalized within the context of OCD, and CBT delivered as usual.[23]

An adequate formulation of the symptoms as being part of the OCD, rather than seeking to "rule out" forensic and sex-offending factors is crucial and requires a good knowledge of the phenomenology of the disorder.[23] Professionals need to be confident in explaining to sufferers that they are not going to act on their obsessive thoughts.[23] Many factors can help differentiate the intrusive sexual thoughts of people with OCD from those of sexual offenders. For example, people with OCD are distressed and disgusted by their thoughts (they are ego-dystonic) and usually try to avoid situations that trigger them. They make efforts to suppress the thoughts, fail to act on or masturbate to them, and very often have additional obsessive-compulsive symptoms.[23] By contrast, a pedophile is likely to regard sexual thoughts as ego-syntonic, to be more ambivalent about having such thoughts and to find them attractive at least some of the time, or to be cautious about revealing their true feelings.[41]

It may sometimes be difficult to assess ego-dystonicity in young people with OCD, as youth are often still in the process of sexual development and maturation.[42] Patients may therefore feel very confused as to whether a sexual thought is wanted or unwanted, permitted, or deviant. The young person may lack the cognitive maturity to identify thoughts as unwanted or may feel that if they admit to wishing they did not have symptoms, they may be asked to stop ritualizing, which they fear would be difficult and anxiety provoking.[23] However, apparent absence of ego-dystonicity or insight does not exclude the diagnosis of OCD, especially in youth.

Some patients with sexual obsessions may report that they feel aroused in response to their unwanted thoughts or images, leading to the interpretation that actually they are sexually deviant. However, people with OCD may be especially sensitive and may consequently over-report arousal.[43] Moreover, selective attention and feedback on the degree of arousal may increase both genital blood flow and the level of arousal. This is not an indication of sexual interest, but of anxiety.[23,43] Additionally, contrary to the arousal that indicates sexual attraction, the arousal that stems from unwanted sexual thoughts is generally accompanied by overt and covert ritualizing.[43] These compulsions may include monitoring arousal levels to determine attraction, maintaining sufficient physical distance from others to ensure that inappropriate touching does not occur, or mental reassurance that one is not sexually deviant.[44]

The misidentification of potential or apparent risk issues in young people with OCD can impede successful treatment outcome for several reasons. First, therapists can become distracted from the OCD, focusing instead on extensive risk assessments, managing the risk itself, or misconceptualizing the risk as a separate or comorbid problem. Second, therapists can misguidedly take measures to reduce apparent risk that are actually counterproductive in terms of tackling OCD, by feeding into obsessional worries. For example, they may alert social services to their concerns, thus reinforcing the patient's belief that they may act on their obsessions and cause harm (see Table 1). Third, therapists may refrain from engaging patients in ERP tasks for fear of increasing apparent risk, or even actively encourage avoidance of situations that trigger sexual or aggressive obsessions, which means that the patient is prevented from accessing the most helpful treatment. A teenager with distressing obsessions about sexual behavior with young children may have developed a highly avoidant profile, e.g. not leaving the house when children are around, dropping out of school, not hugging their younger relatives, and

discontinuing their baby-sitting job. Treatment in this example must actively incorporate graded exposure to children and babies, including a robust family understanding that the teenager is not going to act on the thoughts. Clinicians are aware that, in order to optimize the effectiveness of exposure-based CBT, particular techniques are required (such as in vivo exposure, incorporating the most distressing triggers into the hierarchy, working closely with family, and reducing/eliminating reassurance) and a less confident or inadequately supervised therapist may be especially reluctant to use the full range of strategies with a child with sexual obsessions.[45]

LIMITATIONS

This study is not without limitations. First, the study was conducted in a specialist clinic receiving referrals for complicated, severe, or treatment refractory OCD, and hence the results may not generalize to other samples. Second, diagnoses were made without using structured diagnostic interviews, as the data were collected as part of a routine clinical service. Third, although in most cases medication was started and had reached a stable dose before CBT commenced, some patients were prescribed new medications or their doses changed during the CBT, according to clinical needs, although this was a relatively rare occurrence. Finally, our findings should be seen as exploratory given the relatively large number of statistical analyses performed.

CONCLUSIONS

Sexual obsessions are common in youth with OCD, even in prepubertal patients. Although these symptoms may be associated with particular clinical features, they do not interfere with treatment response. Clinicians, families, and society at large should be educated about the benign nature of sexual obsessions to prevent any catastrophic misinterpretation of these symptoms as posing a risk to others and to provide a message of optimism regarding the chances of recovery.

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DISCUSSION

3. DISCUSSION

In the present chapter, a summary of the discussion for each of the studies included in this thesis will be offered. Following this, comments on the limitations of these works will be provided. Finally, a general discussion focusing on how these research studies contribute to the broader area of OCD and future lines of research will be outlined.

3.1. STUDIES DISCUSSION

3.1.1. STUDY 1: Temporal stability of the OCD symptoms in children and adolescents

This study examined the temporal stability of OCD symptoms in a pediatric sample of OCD patients. Outcome data, gathered an average of 5 years following initial assessment, indicated that the majority of participants maintained their symptoms between baseline and follow-up, demonstrating temporal stability of symptoms. Some variability was observed *within* particular symptom categories. In the majority of these cases, symptoms went from present at baseline to absent at follow-up rather than from absent to present, suggesting that the emergence of new symptoms is less common. When individual symptom categories were grouped into the four previously identified OCD symptom dimensions (*Cleaning*, *Forbidden thoughts*, *Hoarding*, and *Symmetry*) all remained stable between baseline and follow-up, with the exception of the *Cleaning* dimension. These findings are consistent with results from the pediatric study by Delorme et al. (2006), which also found that the contamination/cleaning dimension decreased significantly at follow-up while the other dimensions remained unchanged.

Interestingly, when patients in remission at follow-up were excluded from the current analyses, no significant changes were seen on any of the individual symptom categories or the symptom dimensions. Together with the fact that most observed changes were from present to absent, rather than the other way around, it is suggested that remission status explains most of the observed changes. As not all these patients were treated at our clinic, it is unclear to what extent these changes were due to treatment effects, spontaneous remission, or other life events during the follow-up period. Additional exploratory correlation analyses showed that variables such as the age of the participants and the length of the follow-up did not correlate with the changes found within each dimension, suggesting that these variables did not have an effect on the stability of the dimensions over the time.

Shifts *between* symptom dimensions did not occur and, indeed, it was found that the best predictor of endorsing a particular symptom dimension at follow-up was having endorsed the same dimension at baseline. The only significant cross-dimensional correlation was found between the *Symmetry* dimension at baseline and the *Hoarding* dimension at follow-up, although this association was small in magnitude. Nevertheless, the finding may have some significance as the excessive

accumulation of objects in OCD is often considered to be secondary to symmetry or just-right concerns (Pertusa, Frost, & Mataix-Cols, 2010; Pertusa et al., 2008).

It is worth noting that, in this study, the partial correlation coefficients were weaker than those reported in the adult studies (Mataix-Cols, Rauch, et al., 2002; Rufer et al., 2005), and more similar to those presented in the pediatric study by Delorme et al. (2006). This suggests that, despite the fact that the best predictor of a future symptom is having had the same symptom in the past, the predictive power of this association is stronger for adult, rather than pediatric, samples. The reasons for this are unclear, possibly relating to a number of factors including measurement error, difficulties separating developmentally normal rituals and symptoms of OCD, as well as the above-mentioned role of clinical remission. Alternatively, it is possible that other developmental factors may partly explain these findings. For example, subjective distress and egodystonia require a certain degree of self-understanding and abstract thinking that may not be sufficiently developed at the time of the initial assessment and which may develop over follow-up or as part of the treatment process. It cannot be fully ruled out, however, that the content of OCD symptoms may be less stable in children/adolescents than it is in adults. It is possible that the phenotypic presentation of OCD is more fluid early on and that, as the brain matures, the specific symptom presentation may progressively become more fixed in adult life.

Overall, the results of this investigation are remarkably consistent with previous longitudinal studies that have employed similar designs in adult clinical (Mataix-Cols, Rauch, et al., 2002; Rufer et al., 2005) and non-clinical samples (Fullana et al., 2009; Fullana et al., 2007; Novara et al., 2011), as well as previous pediatric research (Delorme et al., 2006). Taken together, our results are in agreement with the notion that the *severity* rather than the *content* of the symptoms fluctuates over time, potentially determining which symptoms patients are more likely to report to clinicians during a given psychiatric assessment. This fluctuation may give the impression of symptom change. This finding does not, however, mean that the emergence of new symptoms is impossible, particularly early on in the course of the disorder. Indeed, exactly when OCD symptoms appear for the first time in very young children is not well understood, partially due to the overlap in developmentally-normal ritualistic behavior and OCD symptoms. It is possible, however, that normal ritualistic behavior and OCD symptoms may be etiologically linked (Bolton et al., 2009).

The finding that the major symptoms of OCD are temporally stable further supports the notion of etiologically independent symptom dimensions that overlap in various degrees in any given patient (Mataix-Cols et al., 2005). This temporal stability may be at least partially explained by genetic factors, as indicated by longitudinal twin studies (van Grootheest, Bartels, et al., 2007; van Grootheest, Cath, Beekman, & Boomsma, 2007). Therefore, there is considerable merit in pursuing this line of research, as a full understanding of OCD is unlikely to be achieved without taking this heterogeneity into account.

The information provided by this study also has clinical implications. For example, the knowledge that most patients' symptom content remains fairly stable over time may potentially aid

relapse prevention strategies. Informing young people and their parents that, should a relapse occur, it is likely to take a form similar to the symptoms observed in the past, can assist families with identifying the early signs of a potential relapse to promote a quick and appropriate clinical action. Families should also be informed that other *de novo* symptoms may also emerge, though this scenario is far less likely.

3.1.2. STUDY 2: Sexual obsessions in children and adolescents with OCD

This study explored sexual obsessions in a large sample of pediatric patients with OCD. Findings indicated that these symptoms are not only common, with more than one in four young people with OCD reporting sexual obsessions, but are also associated with marginally higher symptom severity and more severe levels of depression. This association between sexual obsessions and depressive mood is in line with a trend found by Grant et al. (2006) in an adult sample, and is also consistent with older literature suggesting that depressed mood is primarily related to obsessions, rather than compulsions, in OCD (Ricciardi & McNally, 1995).

As it has been shown in adult samples, sexual obsessions in this study tended to appear alongside other symptoms from the *Forbidden thoughts* dimension, and also alongside magical thinking, fear of saying certain things, and compulsions such as repeating rituals, superstitious games, mental rituals, and the need to tell, ask, or confess (Bloch et al., 2008; Mataix-Cols et al., 2005).

Young people with sexual obsessions were marginally, yet significantly, older than those without sexual obsessions. Similarly, Geller et al. (2001) reported a higher proportion of sexual obsessions in adolescents with OCD, compared to children and adults. In our sample, sexual obsessions were particularly common in children aged 15 or older. However, these obsessions were also present in much younger children (as young as 8 in our sample).

Contrary to some of the previous literature (Alonso et al., 2001; Mataix-Cols, Marks, et al., 2002; Olino et al., 2011; Rufer et al., 2006), patients with sexual obsessions were just as likely to respond to developmentally-tailored CBT as patients without such symptoms. This was true independently of whether the patients were on SRI medication or not, and taking into account that patients with sexual obsessions were slightly more likely to be on medication.

Patients with sexual obsessions were more likely to receive treatment at the national and specialist OCD clinic (rather than being sent back to their local teams for treatment), being the reasons for this unclear. Individuals with sexual obsessions were more severely impaired and more depressed, so it may be that clinicians felt that both CBT and medication were needed to achieve optimal response. To our knowledge, there is no strong evidence to suggest that patients with more severe obsessions (sexual or otherwise) are more likely to benefit from a combined treatment of CBT plus SRI vs. CBT alone, unless there is a clear clinical indication such as severe depression or suicidal risk. An alternative, perhaps not incompatible, explanation may be that patients, families,

and professionals are more alarmed by such symptoms and therefore specialist treatment is seen as the safest, most assertive option.

Sexual obsessions can be alarming and distressing for both families and clinicians, as they may erroneously be perceived to indicate a potential risk to others. This may lead to unnecessarily lengthy and damaging risk assessments, which may in turn provoke greater distress, rituals, avoidance, and mistrust of health professionals. An adequate formulation of the symptoms as being part of the OCD, as opposed to being related to forensic and sex-offending factors, is crucial and requires a good knowledge of the phenomenology of the disorder (Veale, Freeston, Krebs, Heyman, & Salkovskis, 2009). Such knowledge is essential for professionals, who need to be confident in assuring sufferers that they are not going to act on their obsessive thoughts (Veale et al., 2009).

Many factors can help differentiate the intrusive sexual thoughts of people with OCD from those of sexual offenders. For example, people with OCD are distressed and disgusted by their thoughts (they are ego-dystonic) and usually try to avoid situations which trigger them. They make efforts to suppress the thoughts, fail to act on or masturbate to them, and very often have additional obsessive-compulsive symptoms. By contrast, a pedophile is likely to regard sexual thoughts as ego-syntonic, to be more ambivalent about having such thoughts, to find them attractive at least some of the time, and to be cautious about revealing their true feelings (Veale et al., 2009).

It may sometimes be difficult to assess ego-dystonicity in young people with OCD, as youth are often still in the process of sexual development and maturation (Geller, 2006). Patients may therefore feel very confused as to whether a sexual thought is wanted or unwanted, permitted or deviant. The young person may lack the cognitive maturity to identify thoughts as unwanted or may feel that if they admit to wishing they did not have symptoms, they may be asked to stop ritualizing, which they fear would be difficult and anxiety-provoking (Veale et al., 2009). However, apparent absence of ego-dystonicity or insight does not exclude the diagnosis of OCD, especially in youth.

Some patients with sexual obsessions may report that they feel aroused in response to their unwanted thoughts or images, leading to interpretations of sexual deviance. However, people with OCD may be especially sensitive and may consequently over-report arousal (Warwick & Salkovskis, 1990). Moreover, selective attention and feedback on the degree of arousal may increase both genital blood flow and the level of arousal. This is not an indication of sexual interest, but of anxiety (Veale et al., 2009; Warwick & Salkovskis, 1990). Additionally, contrary to the arousal that indicates sexual attraction, the arousal that stems from unwanted sexual thoughts is generally accompanied by overt and covert ritualizing (Warwick & Salkovskis, 1990).

The misidentification of potential or apparent risk issues in young people with OCD can impede successful treatment outcome for several reasons. First, therapists can become distracted from the OCD, focusing instead on extensive risk assessments, managing the risk itself, or misconceptualising the risk as a separate or comorbid problem. Second, therapists can misguidedly take measures to reduce apparent risk, and thereby essentially feed into the patient's obsessional worries. Third, therapists may refrain from engaging patients in ERP tasks for fear of increasing

apparent risk, or even actively encourage avoidance of situations that trigger sexual obsessions, which means that the patient is prevented from accessing the most helpful treatment.

3.2. LIMITATIONS

Limitations of the studies are detailed in the respective publications enclosed in *Chapter 2*. However, those common to both pieces of research are also listed here.

Both studies were conducted in a national and specialist clinic receiving referrals for complicated, severe, or treatment refractory OCD. Moreover, the professionals delivering treatment at this clinic are highly trained and experienced clinicians. Both facts may limit the generalization of our results to other samples and clinical settings. However, it should be noted that our findings were overall consistent with studies carried out in alternative populations, suggesting that the impact of these factors may not be significant.

An additional weakness across studies concerns the diagnostic procedures used. As the data were collected as part of routine clinical service, participants' diagnoses were made according to the criteria of the clinicians involved in the assessments, and structured diagnostic interviews were not used to confirm the clinicians' judgments. While this type of diagnostic confirmation would be empirically ideal, the approach used reflects the reality of daily clinical practice and ultimately enabled the investigation of outcomes in a relatively large number of unselected young people with OCD.

Also in relation to the assessment strategies, another limitation was the use of the CY-BOCS-SC to assess the presence/absence of OCD symptoms and symptom dimensions. The Y-BOCS-SC, which is the adult version of this instrument, has shown a number of psychometric shortcomings (e.g., Mataix-Cols, Fullana, Alonso, Menchon, & Vallejo, 2004), including a generally poor convergent validity. While another study focusing on the psychometric properties of the CY-BOCS-SC (Gallant et al., 2008) found that the convergent validity of the instrument ranged from good to excellent, this work employed only one measure of convergence – the Anxiety Disorders Interview Schedule for DSM-IV: Parent Version (Silverman & Albano, 1996). On the other hand, in *Study 1*, our analyses used the *a priori*–defined symptom categories of the CY-BOCS-SC rather than the individual symptoms. Each of these categories of symptoms includes different numbers of items. This is especially relevant as categories including a higher number of items could be more likely to appear to change over time. However, results remained largely unchanged when using the mean number of items/categories endorsed within each category/dimension as opposed to their sum. The use of instruments capable of encompassing the dimensionality of obsessive-compulsive symptoms could ease these restraints.

3.3. IMPLICATIONS FOR RESEARCH AND FUTURE DIRECTIONS

In the present thesis, we studied young people with OCD in a naturalistic setting to address two empirical questions. First, we aimed to examine the temporal stability of obsessive-compulsive symptoms and symptom dimensions. Second, we wanted to study the characteristics and treatment outcomes of young individuals with sexual obsessions, a common presentation of OCD. The conclusions of these studies (thoroughly discussed above in Section *3.1. Studies discussion*) reinforce the conceptualization of OCD as a broad, phenotypically heterogeneous entity that is manifested in this way throughout all developmental stages.

Given the amount of data available, which includes the studies here presented, the phenotypic heterogeneity of OCD remains unquestionable. Importantly, the observed heterogeneity of the disorder has been shown to reflect distinct or partially distinct etiologic mechanisms (e.g., Iervolino et al., 2011). Therefore, considering OCD as a unitary entity could obscure the findings from studies attempting to understand the psychological and biological mechanisms implicated in OCD and hamper progress in developing new treatment strategies for this chronic, disabling condition (Iervolino et al., 2011). An approach which adequately considers the heterogeneity of the disorder as well as the developmental framework will improve our understanding of OCD and allow the recognition of more refined phenotypes for future studies examining etiology, pathophysiology, and treatment for OCD. Some promising areas of research that, within this scope, have the potential to advance the field are discussed below.

3.3.1. Refinement of available assessment tools

As mentioned in the *Limitations* section above, the dimensional approach to OCD depends on the *a priori* structure of the field's primary symptom measure: the Y-BOCS-SC (and its children and adolescent version, the CY-BOCS-SC). This comprehensive list classifies more than 50 common obsessions and compulsions into 13 major symptom categories based on the symptoms' overt similarities. In addition, two "miscellaneous" categories are provided to address obsessions and compulsions which are not adequately captured by these major divisions. Most factorial studies to date have used composite scores on these *a priori* categories rather than individual symptoms. However, it has been suggested that these studies are biased as they assume the validity of these symptom groupings, restrict the number of items available for analysis, and limit the symptom dimensions that can emerge (Denys, de Geus, van Megen, & Westenberg, 2004; Summerfeldt, Richter, Antony, & Swinson, 1999). Despite these significant weaknesses, category-level factor analyses have been applied to the Y-BOCS-SC for practical reasons (e.g., fewer variables to manage, smaller samples required for power than item-level analyses) (Pinto et al., 2008). Reassuringly, item-level analyses of the Y-BOCS-SC have yielded fairly similar factor solutions that correspond to the widely accepted and long held themes of OCD (Denys et al., 2004; Katerberg et al., 2010; Pinto et al., 2008). However, there is still a need for a psychometrically sound, clinician-administered scale, which is able to measure both the global severity of OCD as well as the severity of its major

symptom dimensions (Pertusa, Fernández de la Cruz, Alonso, Menchon, & Mataix-Cols, 2012). The Dimensional Y-BOCS (DY-BOCS) (Rosario-Campos et al., 2006), has been developed to meet these needs. Unfortunately, this instrument was not available at the time the current studies were designed. Future studies may also benefit from multi-method, multi-informant approaches to symptom measurement, such as combining self-report with parental and clinician report in order to fully capture the patients' symptoms. This may be particularly relevant with very young children, who may not be able to provide accurate self-report. Similarly, parents may be confused about the difference between normal and abnormal phenomena.

3.3.2. Methodological implications: longitudinal, genetic, and imaging studies

Longitudinal studies examining variations in obsessive-compulsive symptoms, comorbidity patterns, brain circuits, and environmental risk factors are very much needed, particularly when linked with the ability to explore potential genetic determinants (Leckman, Bloch, & King, 2009). Longer longitudinal studies would help to understand the long-term course of OCD symptom dimensions, from childhood to adulthood. Longitudinal analyses could also have important implications in refining therapeutic decisions; for example, identifying dimension-specific predisposing or maintaining factors that could be targeted in treatment. Similarly, following up high-risk individuals who do not develop psychopathology may be especially valuable in elucidating protective factors (Iervolino et al., 2011; Leckman et al., 2009; Mataix-Cols, 2006).

Twin and family studies have proven to be particularly useful in clarifying the etiological structure underlying the symptom dimensions and the heterogeneous nature of OCD (Iervolino et al., 2011; van Grootheest, Bartels, et al., 2007; van Grootheest, Cath, et al., 2007). Indeed, in a recent twin study on OCD symptom dimensions (Iervolino et al., 2011), the authors examined shared versus unique genetic and environmental factors across symptom dimensions. Findings indicated a substantial etiological overlap across dimensions, as well as dimension-specific genetic and environmental factors conferring risk to the individual expressions of the disorder. Moving forward, further research is warranted for detecting the genetic susceptibility loci that may contribute to the expression of the varied OCD symptomatology (Leckman et al., 2009).

Similarly, functional neuroimaging studies have the potential to provide further validation of the dimensional approach to OCD. Studies conducted to date show that OCD symptoms are mediated by abnormal activity in specific orbitofronto–striatal–pallidal–thalamic circuits (Saxena & Rauch, 2000). However, a possible confounder within existing imaging studies is the inclusion of subjects with different OCD symptoms, which may lead to inconsistent findings in groups of patients with variant symptom profiles. Mataix-Cols, Wooderson, et al. (2004) used a symptom provocation paradigm to examine the neural correlates of different OCD symptom dimensions and found that each of the studied dimensions was mediated by distinct but partially overlapping neural systems. For example, hyperactivations in the bilateral ventromedial prefrontal regions and right caudate nucleus were observed in association with washing symptoms, as opposed to a

greater involvement of putamen/globus pallidus, thalamus, and dorsal cortical areas for checking symptoms, and the left precentral gyrus and right orbitofrontal cortex for hoarding symptoms. Another study (Lawrence et al., 2007) demonstrated that patients with predominant washing symptoms showed greater activation in the left ventrolateral prefrontal cortex when shown disgusting faces, compared with non-washing OCD patients and healthy controls. Given that research suggests that different symptom dimensions may have distinct neural substrates, further research in carefully selected, more homogeneous samples is needed. A number of high quality imaging studies employing various modalities, such as voxel-based morphometry (van den Heuvel et al., 2009) and resting state connectivity (Harrison et al., 2013) is beginning to emerge. It is anticipated that the next few years will see a much more accurate mapping of the common and distinct neural systems implicated in each of the major dimensions of OCD.

3.3.3. Treatment implications

Additional work is required to ensure that the accumulated knowledge about OCD and the mechanisms underlying this condition is translated into effective interventions for tackling this disorder. Therapeutic interventions should, ideally, be tailored to specific dimensions, populations, and developmental stages. However, in this regard, there remains considerable room for improvement.

For example, treatment manuals for OCD have tended to address symptoms at a general level, as it would be difficult to include detailed approaches for each possible symptom in a single manual (Sookman, Abramowitz, Calamari, Wilhelm, & McKay, 2005). However, given the empirical differences in phenomenology, cognitions, and even number of required sessions, manuals focused on specific symptom dimensions may facilitate improved treatment outcomes. Although ERP for all forms of OCD uses the same principles, it could be helpful for clinicians to have intervention materials with highly relevant examples of exposures and information about research findings specific to the type of OCD being treated (Williams et al., 2013).

Similarly, given the high comorbidity rates seen in individuals with OCD, it is important to examine what impact comorbidities have on treatment (Steketee, Chambless, & Tran, 2001; Storch et al., 2008). For example, having primary OCD with comorbid Posttraumatic Stress Disorder has been found to decrease response rate (Gershuny, Baer, Jenike, Minichiello, & Wilhelm, 2002), while OCD and comorbid Generalized Anxiety Disorder has shown to increase dropout rates and decrease treatment response (Steketee et al., 2001). In contrast, other studies have shown no negative impact on OCD treatment due to comorbid anxiety problems in adults (Steketee et al., 2001) or children (Storch et al., 2008). More research concerned with the impact of comorbidity patterns on treatment selection and outcomes is required, to ensure that the most optimal therapeutic methods are employed (Steketee, Eisen, Dyck, Warshaw, & Rasmussen, 1999). Likewise, comorbid conditions other than anxiety disorders should be explored. For example, OCD is a frequent comorbid condition in young people and adults with Autism Spectrum Disorders (ASD) (Russell,

Mataix-Cols, Anson, & Murphy, 2005; South, Ozonoff, & McMahon, 2005). A recent study (Russell et al., 2013) showed that CBT for OCD in a group of adults and adolescents with ASD was effective to treat comorbid OCD in this population. Again, these studies should also be extended to younger patients.

Another relevant issue is the dissemination of known treatments. It has been documented that, despite the efficacy of the available interventions for OCD, the majority of individuals suffering from this condition are not receiving appropriate treatment (Kohn, Saxena, Levav, & Saraceno, 2004; Regier et al., 1993). One study found that only 45.1% of individuals with the disorder received relevant services and as few as 25% were under specialty care (Regier et al., 1993). In a British study conducted in 2000, only 5% of adults with OCD actually received CBT (Torres et al., 2007) and similar numbers have been found in the United States (Blanco et al., 2006) and in Spain (Fernández et al., 2006). Furthermore, public awareness of OCD is lower than awareness of other disorders (Torres et al., 2006). Barriers to treatment should be identified and tackled to encourage help-seeking among individuals with OCD (Marques et al., 2010). In the case of lack of access to CBT, it has been proposed that one of the barriers is the lack of CBT therapists within the health care system (Mataix-Cols & Marks, 2006; Shapiro, Cavanagh, & Lomas, 2003). Developing new treatment delivery formats, such as telephone-based or internet-based CBT (Andersson et al., 2012; Turner, Heyman, Futh, & Lovell, 2009), could increase accessibility of CBT with sustained efficacy.

3.3.4. Beyond Obsessive-Compulsive Disorder

The multidimensional model of OCD and the study of its phenotypes according to the methods described above has not only led to the conceptualization of OCD as a heterogeneous condition, but also to a refinement of its nosology and relationship to other related conditions. The most obvious example is hoarding. The "inability to discard worn-out or worthless objects even when they have no sentimental value" became a core diagnostic criterion for Obsessive-Compulsive Personality Disorder (OCPD) only since DSM-III-R. In 1994, DSM-IV introduced the idea that "extreme" hoarding might in fact warrant a diagnosis of OCD, leading to the widespread conceptualization of hoarding as a symptom (or symptom dimension) of OCD (Mataix-Cols et al., 2010). Clearly, in some cases, hoarding can be considered a symptom of OCD (Pertusa et al., 2010; Pertusa et al., 2008; Samuels et al., 2007), but research conducted in the last decade has shown that the majority of severe hoarding cases do not meet criteria for other Axis I or Axis II disorders, lending support to the idea that hoarding is best classified as an independent entity. This separate condition is now known as "Hoarding Disorder" and is listed as a new, independent condition in the recently published DSM-5 under the new *Obsessive-Compulsive and Related Disorders* chapter (American Psychiatric Association, 2013; Mataix-Cols et al., 2010).

Very little is known about the causes of Hoarding Disorder and how to best treat it. In keeping with the trend, limited research has been carried out on Hoarding Disorder in young people (e.g., Storch et al., 2011). Nevertheless, it seems an interesting path to pursue given that

several retrospective studies suggest that hoarding symptoms first emerge in childhood or early adolescence, at an average age of 12 – 13 years (e.g., Ayers, Saxena, Golshan, & Wetherell, 2010). However, at this stage it is not clear if the diagnostic criteria can be used in the pediatric population or whether they will require modifications for their implementation in these samples (Mataix-Cols & Pertusa, 2012).

The relationship between OCD and other OCD-related disorders also remains largely under-investigated. For instance, both OCD and Body Dysmorphic Disorder present with an analogous phenomenology as well as a similar pattern of gender distribution, onset, comorbidity, course of illness, and treatment response (Phillips, Wilhelm, et al., 2010). Moreover, a twin study demonstrated a substantial genetic overlap between the two conditions, especially between body dysmorphic concerns and the *Symmetry* dimension (Monzani et al., 2012). More research however is needed to clarify the etiological links between the different symptom dimensions and OCD-related disorders. A deeper study of all obsessive-compulsive spectrum disorders and efforts to clarifying patterns of comorbidity and shared etiology between them would have important clinical implications for assessment and treatment approaches as well as for guiding future research. Comparisons with other OCD-related disorders are also necessary, especially to help delineating the nosology of these disorders. In this line, Monzani, Rijsdijk, Harris, and Mataix-Cols (submitted for publication) have very recently conducted a twin study estimating the degree to which OCD, Body Dysmorphic Disorder, Hoarding Disorder, Trichotillomania (Hair-Pulling Disorder), and Excoriation (Skin-Picking) Disorder share genetic and environmental risks factors. They concluded that obsessive-compulsive and related disorders may be influenced by two distinct, rather than a single, liability factors, with one of these factors common to all disorders, and another exclusive to Trichotillomania and Excoriation Disorder. Disorder-specific genetic factors unique to OCD, Body Dysmorphic Disorder, and Hoarding Disorder were also apparent, whereas Trichotillomania and Excoriation Disorder were largely influenced by the same latent genetic factors. Studies using the same methodological approach focusing on the different OCD dimensions are warranted.

CONCLUSIONS

4. CONCLUSIONS

This thesis aimed to study unexplored clinical features of pediatric OCD, taking into account the clinical heterogeneity of the disorder, using a large sample of children and adolescents with OCD. We focused on 1) the study of the temporal stability of OCD symptoms and symptom dimensions in childhood and adolescence and 2) exploring the features and treatment outcomes of sexual obsessions in this age group.

The main conclusions of the thesis, derived from *Study 1* (I, II, III) and *Study 2* (IV, V, VI), as well as the significance of the results (VII) and future lines of research that could be pursued (VIII), can be summarized as follows:

I. The content of OCD symptoms and symptom dimensions in young people is relatively stable across time and spans well into early adulthood.

II. Additional variables, such as the age of onset of the OCD or the severity of the symptoms, do not seem to have an effect on the stability of the symptom dimensions.

III. Most changes that occur in symptoms do so *within* rather than *between* symptom dimensions and are largely attributable to clinical remission.

IV. Around one in four children and adolescents with OCD present with sexual obsessions. These obsessions are more common in adolescents, but are also present in pre-pubertal patients.

V. Sexual obsessions are associated with particular clinical features such as presence of more depressive symptoms and slightly more severe OCD.

VI. Importantly, the presence of sexual obsessions does not interfere with response to CBT treatment (with or without medication).

VII. The results of both studies reinforce the conceptualization of OCD as a broad, phenotypically heterogeneous entity that is manifested in this way throughout all developmental stages.

VIII. Future lines of research that, within this scope, have the potential to advance the field of OCD and its related disorders include: 1) the refinement of OCD assessment tools; 2) longitudinal, genetic, and imaging studies using larger samples; and 3) tailoring treatments to specific symptom dimensions, populations, and developmental stages.

SUMMARY OF THE THESIS IN CATALAN

(RESUM DE LA TESI)

CLINICAL HETEROGENEITY OF OBSESSIVE-COMPULSIVE DISORDER IN CHILDREN AND ADOLESCENTS: TEMPORAL STABILITY AND TREATMENT OUTCOMES

5. SUMMARY OF THE THESIS IN CATALAN

(RESUM DE LA TESI)

HETEGORENEÏTAT CLÍNICA DEL TRASTORN OBSESSIVOCOMPULSIU EN NENS I ADOLESCENTS: ESTABILITAT TEMPORAL I RESPOSTA AL TRACTAMENT

INTRODUCCIÓ

TRASTORN OBSESSIVOCOMPULSIU PEDIÀTRIC

El Trastorn Obsessivocompulsiu (TOC) és un trastorn psiquiàtric inclòs al Manual Diagnòstic i Estadístic de Trastorns Mentals, 5a edició (DSM-5). Tot i que el TOC pediàtric té algunes peculiaritats, no difereix massa del TOC adult pel que fa a la seva presentació fenomenològica. Com en el cas dels adults, el TOC en nens i adolescents es caracteritza per la presència d'obsessions o compulsions o, de manera més comú, de tots dos fenòmens. Les obsessions es defineixen com pensaments, impulsos o imatges que es viuen com intrusius i no desitjats i que produeixen ansietat en l'individu que les pateix. Per la seva banda, les compulsions són conductes repetitives o actes mentals que la persona afectada se sent obligada a fer en resposta a una obsessió amb l'objectiu de prevenir o reduir l'ansietat, o prevenir alguna situació no desitjada. Aquestes conductes o actes mentals no estan connectats de manera realista amb l'esdeveniment que volen neutralitzar o evitar, o són clarament excessius. El DSM-5 especifica que els nens més petits poden no ser capaços de definir la finalitat d'aquestes conductes (American Psychiatric Association, 2013). En el cas del nens, també és important en diagnosticar un TOC el saber diferenciar els rituals normals que tenen lloc durant el desenvolupament de les compulsions (Abramowitz et al., 2009; Leckman & Bloch, 2008). En el context del desenvolupament normal, aquests rituals tendeixen a ser transitoris, ajuden a manejar l'ansietat i tenen un paper en la socialització de l'individu. En canvi, els rituals en el TOC tenen una aparició més tardana, generen ansietat si no es fan, són egodistònics i incapacitants (Leonard et al., 1990; Swedo et al., 1989).

El TOC és un dels trastorns psiquiàtrics més comuns, amb prevalences en el rang de l' 1 al 3% en la població general, sent aquestes ràtios similars tant en poblacions pediàtriques com en adultes (Flament et al., 1988; Fontenelle et al., 2006; Ruscio et al., 2010; Zohar, 1999). Aproximadament la meitat dels pacients adults amb TOC informen de que l'inici de la malaltia es va produir durant l'edat infantil (Stewart et al., 2004). L'inici del trastorn és normalment gradual, i la gravetat dels símptomes generalment canviarà al llarg del temps, sovint en resposta a estressors vitals (Mataix-Cols, Rauch, et al., 2002; Stewart et al., 2004). Si no es tracta, el curs del TOC tendeix a ser crònic (Ravizza et al., 1997; Skoog & Skoog, 1999). Alguns individus presenten un curs episòdic,

i una minoria tenen un curs deteriorant. Per una proporció substancial dels pacients amb inici del trastorn a la infància, el TOC persisteix fins a l'edat adulta (Micali et al., 2010).

Al voltant del 75% dels nens i adults amb TOC tenen un o més d'un diagnòstic comòrbid (Fireman et al., 2001). En adults, les comorbiditats més freqüents són els trastorns d'ansietat i la depressió (Torres et al., 2006), mentre que en els nens les comorbiditats tendeixen a ser condicions més conductuals, en especial el Trastorn per Dèficit d'Atenció amb Hiperactivitat o el Trastorn Negativista Desafiant (Leonard et al., 2001). Addicionalment, fins a un 30% de pacients amb TOC també patiran un Trastorn per Tics al llarg de la vida (American Psychiatric Association, 2013).

Respecte a l'etiologia del trastorn, el TOC ha mostrat ser una condició familiar, moderadament heretable (Mataix-Cols et al., 2013; Pauls, 2010). El trastorn també sembla estar relacionat amb disfuncions del sistema serotoninèrgic (López-Ibor & López-Ibor, 2003) i, més recentment, també s'ha suggerit que els sistemes glutamatèrgics i dopaminèrgics tindrien un paper en la seva gènesi (Camarena et al., 2007; Greist et al., 1995; Wu et al., 2013). Les dades neuropsicològiques, de neuroimatge i els estudis psicofarmacològics suggereixen que els individus amb TOC presenten una disfunció en el còrtex òrbito-frontal, el còrtex anterior cingulat i l'estriat (Kang et al., 2003; Milad & Rauch, 2012; Radua & Mataix-Cols, 2009). S'han descrit dèficits en funcions executives, així com en funcions visuoespacials i psicomotores (Andres et al., 2007; Kuelz et al., 2004; Murphy et al., 2010). En una minoria de casos de TOC (i Trastorns per Tics) d'inici en la infància, s'ha proposat que els símptomes podrien ser conseqüència d'un procés autoinmune post-infecciós. Aquests casos s'agrupen sota la denominació PANDAS (*Pediatric Autoinmune Neuropsychiatric Disorders Associated with Streptococcal Infection* [Trastorns Pediàtrics Autoinmunes Neuropisquiàtrics Associats amb Infecció Estreptocòccica]) (da Rocha et al., 2008).

D'acord amb l'evidència científica disponible (p. ex., Eddy et al., 2004; Foa et al., 2005; Gava et al., 2007; O'Kearney et al., 2006; Soomro et al., 2008; Pediatric OCD Treatment Study (POTS) Team, 2004), els tractaments eficaços i recomanats per al TOC són la Teràpia Cognitivoconductual (TCC) – incloent Exposició amb Prevenció de Resposta (ERP) – i els Inhibidors de la Recaptació de la Serotonina (IRSs).

HETEROGENEÏTAT DEL TRASTORN OBSESSIVOCOMPULSIU

Tant en nens i adolescents com en adults, els símptomes del TOC han demostrat ser notablement heterogenis (Mataix-Cols et al., 2005). Anàlisis factorials en poblacions pediàtriques i adultes han agrupat els símptomes del TOC en diferents dimensions de símptomes. Una metanàlisi dels autors Bloch, Landeros-Weisenberg, Rosario, Pittenger i Leckman (2008) va identificar quatre dimensions de símptomes: 1) *Acumulació*, que comprèn les obsessions i compulsions d'acumulació; 2) *Simetria*, que comprèn les obsessions de simetria i les compulsions d'ordenar, repetir i comptar; 3) *Pensaments prohibits*, que comprèn les obsessions agressives, sexuals, religioses i somàtiques; i 4) *Neteja*, que comprèn les obsessions de contaminació i les compulsions de neteja. Aquesta metanàlisi va comprendre 21 estudis d'anàlisis factorials, incloent 5,124 participants. Quatre

d'aquests estudis van utilitzar mostres pediàtriques, suposant un total de 679 nens i adolescents (Delorme et al., 2006; Mataix-Cols et al., 2008; McKay et al., 2006; Stewart et al., 2007).

L'heterogeneïtat clínica del trastorn planteja la qüestió de si el TOC és també una condició etiològicament heterogènia. En resposta a aquest dubte, s'ha proposat l'existència d'un model multidimensional (Mataix-Cols et al., 2005) en el que el TOC seria considerat un conjunt de síndromes que potencialment, es podrien superposar, més que no pas una entitat unitària. Alguns dels factors etiològics en la base d'aquests síndromes relacionats serien específics a cada dimensió, mentre que altres factors etiològics serien comuns a totes elles. Si aquest model fos acurat, tenir en compte l'heterogeneïtat fenotípica del trastorn milloraria el coneixement de les causes del mateix (Mataix-Cols et al., 2005). A més, aquesta informació ajudaria a desenvolupar tractaments millors i més específics.

Aquest enfocament multidimensional està recolzat per un nombre creixent d'estudis clínics (p. ex., Leckman et al., 1994; Rosario-Campos et al., 2001), evolutius (p. ex., Evans et al., 1999; Evans et al., 1997; Zohar & Felz, 2001), longitudinals (p. ex., Mataix-Cols, Rauch, et al., 2002; Rufer et al., 2005), genètics (p. ex., Iervolino et al., 2011; Katerberg et al., 2010), de neuroimatge (p. ex., Gilbert et al., 2009; Mataix-Cols, Wooderson, et al., 2004; van den Heuvel et al., 2009), i de tractament (p. ex., Mataix-Cols, Marks, et al., 2002; Mataix-Cols et al., 1999; Rufer et al., 2006).

Malauradament, la majoria de la recerca en relació a l'heterogeneïtat del TOC prové d'estudis amb mostres adultes. La recerca en mostres pediàtriques és necessària per validar si les assumpcions que es fan en referència al model multidimensional són també apropiades per a la població de nens i adolescents (Mataix-Cols et al., 2005).

Estabilitat dels símptomes obsessivocompulsius en TOC pediàtric

La validesa de la classificació del TOC basada en símptomes tot just descrita es veuria compromesa si les dimensions de símptomes no fossin temporalment estables; és a dir, si el contingut dels símptomes dels pacients canviés de manera significativa al llarg del temps (Fullana et al., 2007). Mentre sovint es pensa que els símptomes dels pacients amb TOC fluctuen al llarg del temps, en gravetat i en contingut, només uns pocs estudis a data d'avui han estudiat de manera empírica aquesta important qüestió utilitzant instruments psicomètrics moderns.

Els estudis en adults, tant en mostres clíniques (Mataix-Cols, Rauch, et al., 2002; Rufer et al., 2005) com no clíniques (Fullana et al., 2009; Fullana et al., 2007; Novara et al., 2011), han mostrat que les dimensions de símptomes són temporalment estables. En canvi, els pocs estudis en població infantil (Delorme et al., 2006; Rettew et al., 1992) han mostrat resultats inconclusius. En general, com en els adults, sembla que les dimensions de símptomes en nens tampoc es modifiquen al llarg del temps i que els canvis d'una dimensió a l'altra són poc comuns. Tot i això, aquestes assumpcions es basen en estudis amb limitacions metodològiques, incloent mostres petites. Per tant, es necessiten més estudis per examinar l'estabilitat temporal dels símptomes i de les dimensions de símptomes al llarg del curs del desenvolupament. Avaluar l'estabilitat del TOC en una mostra

pediàtrica gran facilitaria un millor enteniment de la progressió dels trastorn, que seria inestimable pels pacients i els seus pares i també pels clínics per tal d'ajudar-los a discernir què esperar en termes d'evolució clínica.

Obsessions sexuals en el TOC pediàtric

Les obsessions sexuals són un símptoma obsessivocompulsiu comú i particularment debilitant. Tant en mostres pediàtriques com d'adults, les anàlisis factorials han trobat que aquestes obsessions s'agrupen sota la dimensió de *Pensaments prohibits*, juntament amb les obsessions agressives i religioses (Bloch et al., 2008). Les obsessions sexuals poden incloure pensaments no desitjats sobre tenir sexe amb membres de la família, por a tenir una conducta sexual violenta, pensaments sobre tenir sexe amb animals, o preocupacions sobre l'orientació sexual (Grant et al., 2006; Williams & Farris, 2011). Aquests tipus d'obsessions tendeixen a romandre amagades, sovint perquè els que les pateixen se senten avergonyits explicant els seus símptomes o perquè aquests es poden percebre con inacceptables (Baer, 2001). Tot i això, han mostrat ser força prevalents en el TOC (Mataix-Cols et al., 2008; Ruscio et al., 2010). Alguns estudis han suggerit que les obsessions sexuals són més comunes en adolescents que no pas en la població de nens més joves i en adults (Geller, Biederman, et al., 2001).

En mostres adultes amb TOC s'ha trobat que les obsessions sexuals són més freqüents en homes, normalment van acompanyades d'altres símptomes de la dimensió de *Pensaments prohibits*, van lligades a més sofriment i malestar clínicament significatiu, i a una edat d'inici del TOC més primerenca (p. ex., Geller, Biederman, et al., 2001). Pel que fa a la resposta al tractament, s'han trobat resultats contradictoris, amb alguns estudis suggerint que tenen una resposta més pobra tant a TCC (Alonso et al., 2001; Mataix-Cols, Marks, et al., 2002; Rufer et al., 2006) com a SRIs (Alonso et al., 2001; Shetti et al., 2005), mentre que d'altres estudis no informen de diferències en la resposta al tractament respecte a altres tipus de símptomes obsessivocompulsius (Denys et al., 2003; Erzegovesi et al., 2001; Mataix-Cols et al., 1999; Stein et al., 2007).

En els nens i els adolescents, les obsessions sexuals han estat llargament ignorades. Tot i això, donat que aquestes obsessions poden ser alarmants, malenteses com a indicadores de risc per a tercers, o confoses amb el desenvolupament sexual normal, és important estudiar-les en la població pediàtrica. Un estudi d'aquest tipus permetria un millor enteniment d'aquests símptomes i proveiria recomanacions sobre com abordar-les a la pràctica clínica.

OBJECTIUS I HIPÒTESIS

L'*objectiu general* d'aquesta recerca va ser estudiar característiques poc explorades del TOC pediàtric, tenint en compte l'heterogeneïtat del trastorn, en una mostra de pacients derivats a una clínica nacional i especialitzada en TOC de Londres, Regne Unit. Específicament, els nostres objectius van ser estudiar l'estabilitat temporal dels símptomes obsessivocompulsius (*Estudi 1*) i la

naturalesa de les obsessions sexuals (*Estudi 2*) en una mostra gran de nens i adolescents. Els objectius concrets dels estudis inclosos, així com les hipòtesis, es descriuen a continuació.

Objectius específics

Estudi 1:

- Establir l'estabilitat temporal de les dimensions de símptomes del TOC en nens i adolescents al llarg d'un període de seguiment de 5 anys de mitjana.
- Establir l'impacte de variables addicionals, tals com l'edat d'inici del TOC o la gravetat dels símptomes, en l'estabilitat de les dimensions de símptomes.

Estudi 2:

- Establir la prevalença d'obsessions sexuals en una cohort gran de nens i adolescents amb TOC.
- Examinar les característiques demogràfiques i clíniques dels nens i adolescents amb obsessions sexuals.
- Examinar la resposta al tractament dels pacients amb vs. els pacients sense obsessions sexuals.

Hipòtesis

Estudi 1:

1. En general, les categories de símptomes i les dimensions de símptomes mostrarien estabilitat temporal al llarg del temps de seguiment, de la mateixa manera que s'ha observat en mostres d'adults.
2. Tenir símptomes d'una determinada dimensió a l'avaluació inicial seria el predictor més fort de tenir símptomes de la mateixa dimensió al seguiment.
3. Les dimensions de símptomes romandrien estables després de controlar els efectes del tractament (ja que els canvis en les dimensions de símptomes podrien ser confosos amb una reducció general de la gravetat del TOC atribuïble a la intervenció).

Estudi 2:

1. Les obsessions sexuals serien un símptoma comú a la mostra, i serien més comuns en adolescents que en nens més joves.
2. Els pacients amb obsessions sexuals també presentarien altres símptomes de la mateixa dimensió (pensaments agressius i religiosos). A més, els participants amb obsessions sexuals estarien més deprimits que aquells sense obsessions sexuals.
3. La presència d'obsessions sexuals no estaria associada amb una pitjor resposta al tractament, sempre i quan el tractament sigui dispensat per un equip especialitzat i que estigui adaptat a les necessitats del desenvolupament del nen.

MÈTODES

Estudi 1: Estabilitat dels símptomes obsessivocompulsius en TOC pediàtric

La mostra va consistir en 74 participants diagnosticats de TOC, derivats a la clínica nacional i especialitzada en TOC i trastorns relacionats per nens i adolescents del Maudsley Hospital, Londres, Regne Unit. L'edat mitjana dels participants a la primera avaluació va ser 13.5 anys (desviació estàndard [sd] = 2.6; rang = 8 – 18). Cinquanta participants eren nois (67.7%). A la primera avaluació els participants van ser avaluats amb l'Escala d'Obsessions i Compulsions de Yale-Brown per Nens (CY-BOCS) i el seu llistat complementari de símptomes (CY-BOCS-SC). Les puntuacions en la CY-BOCS van estar en el rang de TOC moderat (mitjana = 22.5, sd = 6.1; rang = 11 – 40). La mostra va a ser avaluada una mitjana de 4.8 anys després de la primera avaluació (sd = 2.8; rang = 1 – 11). Es van utilitzar anàlisis de la variància i models de regressió múltiple per examinar els canvis entre els dos moments temporals (primera avaluació i seguiment) dintre de cada categoria de símptomes i de cada dimensió de símptomes (*Neteja*, *Pensaments prohibits*, *Acumulació* i *Simetria*) i entre les diferents categories de símptomes i les diferents dimensions.

Estudi 2: Característiques i resposta al tractament de les obsessions sexuals en TOC pediàtric

La mostra va estar composada per 383 participants diagnosticats de TOC, derivats a la clínica nacional i especialitzada en TOC i trastorns relacionats per nens i adolescents del Maudsley Hospital, Londres, Regne Unit. L'edat mitjana dels pacients va ser 14.34 anys (sd = 2.24; rang = 7 – 18). Dos-cents setze participants eren nois (56.4%). Tots els participants van ser avaluats una primera vegada i, aquells que van rebre tractament a la clínica (153 participants; 39.9%), van ser també avaluats de nou a l'acabar la intervenció. Per aquest darrer grup, el tractament va consistir en TCC incloent EPR (amb o sense medicació). Les mesures d'avaluació van incloure la CY-BOCS (puntuació mitjana a la primera avaluació = 26.32, sd = 5.65) i la CY-BOCS-SC, així com l'Inventari d'Obsessions i Compulsions per Nens (ChOCI), l'Escala d'Acomodació Familiar (FAS), el Questionari de Punts Forts i Dificultats (SDQ), l'Inventari de Depressió de Beck per a Joves (BDI-Y) i l'Escala d'Avaluació Global per a Nens (CGAS). Els pacients amb i sense obsessions sexuals van ser comparats respecte a característiques socio-demogràfiques i clíniques. Es van utilitzar models mixtes d'anàlisis de la variància per comparar les respostes al tractament d'ambdós grups.

RESULTATS

Estudi 1: Estabilitat dels símptomes obsessivocompulsius en TOC pediàtric

Es van observar canvis dintre de cada categoria de símptoma individual d'obsessions i compulsions en aproximadament un 15% – 45% dels casos. Les obsessions agressives i les compulsions de neteja, comprovació, repetició i ordre van ser les úniques categories de símptomes que van mostrar diferències significatives entre l'avaluació inicial i el seguiment. Tot i que la majoria de canvis van anar de present a l'avaluació inicial a absent en el seguiment, en alguns dels participants la direcció del canvi va ser l'oposada.

Els canvis dins de les dimensions de símptomes entre l'avaluació inicial i el seguiment van ser només significatius per la dimensió *Neteja* (millora dels símptomes) (Wilcoxon test, z = -3.226, p = .001), mentre que la resta de dimensions es van mantenir estables.

Es van dur a terme anàlisis exploratòries addicionals per avaluar si l'edat dels participants a l'avaluació inicial, l'edat d'inici del TOC, la durada de la malaltia i la gravetat global dels símptomes eren predictors significatius del percentatge de canvi en el temps dins de cada dimensió. Els resultats no significatius van suggerir que cap d'aquestes variables va tenir un efecte sobre l'estabilitat temporal de les dimensions de símptomes.

En excloure de les anàlisis aquells participants que el seu TOC havia remès durant el seguiment (n = 42), les diferències observades prèviament en categories de símptomes i en dimensions de símptomes van deixar de ser significatives.

Les anàlisis de regressió múltiple van mostrar que l'únic predictor d'una determinada dimensió de símptomes al seguiment vas ser tenir aquella mateixa dimensió a l'avaluació inicial. L'única excepció va ser la dimensió de *Simetria* a l'avaluació inicial, que va ser addicionalment predictora de símptomes d'*Acumulació* en el seguiment. La magnitud dels coeficients de correlació parcial va ser moderada (rang = .25 – .35). Aquestes magnituds van millorar lleugerament quan es van excloure els 42 participants que ja no complien criteris per al TOC al seguiment (rang = . 22 – .44).

Estudi 2: Característiques i resposta al tractament de les obsessions sexuals en TOC pediàtric

D'acord amb la CY-BOCS-SC, a l'avaluació inicial 102 pacients (26.6%) presentaven obsessions sexuals. En aquest grup, les obsessions sexuals més freqüents van ser els pensaments, imatges o impulsos prohibits o perversos (n = 71, 74.7%).

Els participants amb obsessions sexuals van mostrar ser lleugerament, tot i que significativament, més grans que aquells sense obsessions sexuals (14.8 vs. 14.2 anys, p = .006). Com es preveia, les obsessions sexuals van ser més freqüents en els adolescents (al voltant de 15 anys) que en els nens més joves. No obstant això, es va trobar que les obsessions sexuals estaven presents en totes les edats (rang = 8 – 17).

Com era d'esperar, el grup amb obsessions sexuals també va presentar obsessions agressives i religioses de manera més freqüent que no pas el grup sense obsessions sexuals (ambdues ps < .01). A més, el grup amb obsessions sexuals també va informar de més freqüència de pensament màgic (p = .035) i de la por de dir certes coses de la categoria miscel·lània (p = .022), i de més jocs supersticiosos (p = .017) i altres compulsions de la categoria de miscel·lània (rituals mentals; necessitat de dir, preguntar o confessar; parpellejar o mirar fixament; totes les ps ≤ .001) que els participants sense obsessions sexuals.

Els participants amb obsessions sexuals va mostrar nivells significativament més alts de depressió (p = .024) i, a més, també tenien un TOC lleugerament més greu (p = .024) d'acord amb les puntuacions de la CY-BOCS.

Per aquells que van realitzar tractament a la clínica (n = 153), els models mixtes d'anàlisi de la variància no van trobar diferències en la resposta al tractament dels pacients amb (n = 50) vs. aquells sense (n = 103) obsessions sexuals, independentment de si els pacients estaven també prenent medicació pel TOC o no.

DISCUSSIÓ

A continuació s'ofereix un resum de la discussió de cada un dels estudis inclosos en aquesta tesi, així com les limitacions dels mateixos. Finalment, s'esbossarà una discussió general centrada en com aquests estudis d'investigació contribueixen a l'àmbit del TOC en general, així com futures línies d'investigació.

DISCUSSIONS DELS ESTUDIS PRESENTATS

Estudi 1: Estabilitat dels símptomes obsessivocompulsius en TOC pediàtric

Aquest estudi va examinar l'estabilitat temporal dels símptomes obsessivocompulsius en una mostra de pacients pediàtrics amb TOC. Els resultats van mostrar que la majoria dels participants van mantenir els seus símptomes al seguiment, realitzat una mitjana de 5 anys després de l'avaluació inicial. Es va observar certa variabilitat en determinades categories de símptomes. En la majoria d'aquests casos, els símptomes van anar de presents a la primera avaluació a absents durant el seguiment, i no d'absents a presents, el que suggereix que l'aparició de nous símptomes és menys comú. Quan categories de símptomes individuals es van agrupar en les quatre dimensions de símptomes TOC prèviament identificades (*Neteja*, *Pensaments prohibits*, *Acumulació* i *Simetria*) totes van romandre estables entre els dos moments temporals d'avaluació, amb l'excepció de la dimensió de *Neteja*. Aquests resultats són consistents amb els resultats de l'estudi pediàtric de Delorme et al. (2006), que també van trobar que la dimensió de contaminació/neteja va disminuir significativament durant el seguiment, mentre que les altres dimensions es van mantenir sense canvis.

Curiosament, quan els pacients en remissió durant el seguiment van ser exclosos de les anàlisis, no es van observar canvis significatius en cap de les categories de símptomes individuals o les dimensions de símptomes. Juntament amb el fet que la majoria dels canvis es van observar de símptomes presents a absents, més que no pas d'absents a presents, suggereix que la remissió explica la major part dels canvis observats. Com no tots els pacients van ser tractats a la nostra clínica, no està clar en quina mesura aquests canvis es deuen als efectes del tractament, a la remissió espontània o a altres esdeveniments de la vida durant el període de seguiment.

No es van observar canvis entre dimensions de símptomes i es va trobar que el millor predictor de tenir una dimensió de símptomes en particular en el seguiment era haver-la tingut en l'avaluació incial. L'única correlació creuada significativa entre dimensions va ser entre la dimensió de *Simetria* a l'avaluació inicial i la dimensió d'*Acumulació* en el seguiment, encara que aquesta associació va tenir una magnitud petita. No obstant això, la troballa pot tenir certa importància, ja

que s'ha trobat que l'acumulació excessiva d'objectes en el TOC és sovint secundària a símptomes de simetria o preocupacions "just-right" (Pertusa et al., 2010; Pertusa et al., 2008).

Val la pena assenyalar que, en aquest estudi, els coeficients de correlació parcial van ser més petits que els trobats en estudis d'adults (Mataix-Cols, Rauch, et al., 2002; Rufer et al., 2005) i més similars als presentats en l'estudi pediàtric de Delorme et al. (2006). És possible que la presentació fenotípica del TOC sigui més fluctuant en edats més primerenques i que, a mesura que el cervell madura, la presentació específica dels símptomes es faci progressivament més estable en la vida adulta.

En general, els resultats d'aquesta investigació són molt consistents amb anteriors estudis longitudinals que han utilitzat dissenys similars en mostres clíniques (Mataix-Cols, Rauch, et al., 2002; Rufer et al., 2005) i no clíniques (Fullana et al., 2009; Fullana et al., 2007; Novara et al., 2011) d'adults, així com amb investigacions pediàtriques prèvies (Delorme et al., 2006). La troballa de que els principals símptomes de TOC són temporalment estables dóna suport a la idea de que les dimensions de símptomes són etiològicament independents (Mataix-Cols et al., 2005). Aquesta estabilitat temporal pot ser, almenys parcialment, explicada per factors genètics, tal i com indiquen els estudis longitudinals realitzats en mostres de bessons (van Grootheest, Bartels, et al., 2007; van Grootheest, Cath, et al., 2007).

Els resultats derivats d'aquest estudi també tenen implicacions clíniques. Per exemple, saber que el contingut dels símptomes de la majoria dels pacients es manté força estable en el temps pot ser d'ajuda a l'hora de programar estratègies de prevenció de recaigudes. Informar als joves i als seus pares de que, en cas d'ocórrer una recaiguda, és probable que els símptomes siguin similars als observats anteriorment pot ajudar a les famílies a identificar els primers signes d'una recaiguda potencial i facilitar una intervenció clínica ràpida i adequada. Tot i això, les famílies també han de ser informades de que també poden aparèixer símptomes nous, encara que aquesta situació és molt menys probable.

Estudi 2: Característiques i resposta al tractament de les obsessions sexuals en TOC pediàtric

Aquest estudi va explorar les obsessions sexuals en una àmplia mostra de pacients pediàtrics amb TOC. Els resultats van indicar que aquests símptomes no només són comuns, amb més d'un de cada quatre joves amb TOC informant obsessions sexuals, sinó que també s'associen amb TOC lleugerament més greu i majors nivells de depressió. Aquesta associació entre obsessions sexuals i estat d'ànim depressiu està en línia amb la tendència trobada per Grant et al. (2006) en una mostra d'adults i també és consistent amb literatura més clàssica que suggereix que la depressió en el TOC està relacionada principalment amb obsessions, més que no pas amb les compulsions (Ricciardi & McNally, 1995).

Tal i com s'ha vist en estudis amb adults, les obsessions sexuals en el present estudi van tendir a aparèixer amb altres símptomes de la dimensió de *Pensaments prohibits*, i també juntament amb pensament màgic, por de dir certes coses, i compulsions com repetir, jocs supersticiosos,

rituals mentals i la necessitat de comptar, preguntar o confessar (Bloch et al., 2008; Mataix-Cols et al., 2005). Els joves amb obsessions sexuals eren lleugerament, tot i que significativament, més grans que aquells sense obsessions sexuals. De la mateixa manera, Geller et al. (2001) van informar d'una major proporció d'obsessions sexuals en adolescents amb TOC, en comparació amb nens més joves i adults. En la nostra mostra, les obsessions sexuals van ser particularment comuns en els nens de 15 anys o més grans. No obstant això, aquestes obsessions també van estar presents en nens molt més joves, la qual cosa ressalta la importància de preguntar per aquests tipus de símptomes de manera oberta i directa, fins i tot a nens molt petits.

A diferència d'alguns dels estudis anteriors (Alonso et al., 2001; Mataix-Cols, Marks, et al., 2002; Olino et al., 2011; Rufer et al., 2006), els pacients amb obsessions sexuals van respondre al tractament amb TCC de la mateixa manera que aquells sense obsessions sexuals, independentment de si els pacients estaven prenent IRSs o no.

Les obsessions sexuals poden ser alarmants i preocupants tant per les famílies com pels clíncs, ja que erròniament poden ser percebudes com un risc potencial per als altres. Això pot conduir a avaluacions del risc innecessàriament llargues i nocives, que a la vegada poden provocar una major angoixa, més rituals, evitacions i desconfiança vers els professionals de la salut. Una formulació adequada dels símptomes com a part TOC, enlloc de relacionar-los amb delictes sexuals (p. ex., pedofilia), és crucial i requereix un bon coneixement de la fenomenologia del trastorn (Veale et al., 2009). Hi ha molts factors que poden ajudar a diferenciar els pensaments sexuals intrusius de les persones amb TOC dels pensaments dels delinqüents sexuals. Per exemple, les persones amb TOC viuen els pensaments amb malestar i fins i tot fàstic (els pensaments són egodistònics) i en general tracten d'evitar les situacions que els provoquen. Fan esforços per suprimir els pensaments, no es masturben amb ells i molt sovint tenen altres símptomes obsessivocompulsius. Per contra, els pensaments d'un pedòfil és probable que siguin egosintònics, aquests individus tindran una opinió més ambivalent respecte a aquests pensaments, els poden trobar atractius i excitants (almenys una part del temps) i tindran cura de no revelar-los per por a les conseqüències (Veale et al., 2009).

Identificar erròniament les obsessions sexuals com un possible risc real pot obstaculitzar el tractament per diverses raons. En primer lloc, els terapeutes es poden distreure del TOC i centrar-se en canvi en avaluacions de risc extenses i innecessàries. En segon lloc, els terapeutes poden prendre mesures errònies per reduir l'aparent risc i, per tant, alimentar les preocupacions obsessives del pacient. En tercer lloc, els terapeutes poden abstenir-se de realitzar tasques d'EPR per por d'augmentar aquest risc aparent, o fins i tot estimular activament l'evitació de situacions que desencadenen obsessions sexuals, el que significa que s'impedeix que el pacient accedeixi al tractament més efectiu.

LIMITACIONS

Ambdós estudis es van realitzar en una clínica nacional i especialitzada que rep derivacions de casos de TOC greus, amb comorbiditats diverses o refractaris. D'altra banda, els professionals

tractant aquests pacients són clínics altament especialitzats i amb àmplia experiència en aquests tipus de casos. Tots dos fets poden limitar la generalització dels resultats a altres mostres i entorns clínics. No obstant això, cal assenyalar que els resultats dels estudis van ser, en general, consistents amb els estudis duts a terme en poblacions alternatives, suggerint que l'impacte d'aquests factors podria no ser tan significatiu.

Un altre punt dèbil d'ambdós estudis es refereix als procediments de diagnòstic utilitzats. Les dades van ser recopilades de manera rutinària com a part del servei clínic. Els diagnòstics dels participants van ser realitzats d'acord amb els criteris dels clínics que participen en les avaluacions i no es van fer servir entrevistes estructurades per confirmar els judicis dels professionals. Si bé aquest tipus de confirmació dels diagnòstics seria empíricament ideal, l'enfocament utilitzat reflecteix la realitat de la pràctica clínica diària i en última instància va permetre investigar un nombre relativament gran de casos no seleccionats de joves amb TOC.

També en relació amb les estratègies d'avaluació, una altra limitació va ser l'ús de la CY-BOCS-SC per avaluar la presència/absència de les categories de símptomes i les dimensions de símptomes del TOC. La Y-BOCS-SC, que és la versió per a adults d'aquest instrument, ha demostrat una sèrie de deficiències psicomètriques (p. ex., Mataix-Cols, Fullana, et al., 2004). D'altra banda, les anàlisis de l'*Estudi 1* es van basar en les categories definides a priori de la CY-BOCS-SC i no pas en els símptomes individuals, de manera que cada categoria de símptomes inclou un nombre diferent de ítems. Tot i això, les anàlisis realitzades posteriorment per corregir aquest fet van donar resultats pràcticament idèntics, la qual cosa ens permet confiar en els resultats obtinguts. L'ús d'instruments capaços d'abastar la dimensionalitat dels símptomes obsessivocompulsius podria contribuir a millorar aquestes restriccions.

IMPLICACIONS PER A LA RECERCA I DIRECCIONS FUTURES

En aquesta tesi es van estudiar joves amb TOC en un entorn naturalístic per abordar dues qüestions empíriques. En primer lloc, es va proposar analitzar l'estabilitat temporal dels símptomes obsessivocompulsius i les dimensions de símptomes del TOC. En segon lloc, es van estudiar les característiques i la resposta al tractament dels nens i adolescents amb obsessions sexuals. Les conclusions d'aquests estudis reforcen la conceptualització del TOC com una entitat àmplia i fenotípicament heterogènia que es manifesta d'aquesta manera a través de totes les etapes de desenvolupament.

Donada la quantitat d'informació disponible, incloent els estudis aquí presentats, l'heterogeneïtat fenotípica del TOC és inqüestionable. A més, l'heterogeneïtat dels símptomes observada ha demostrat reflectir també mecanismes etiològics diferents o parcialment diferents per a cada dimensió (p. ex., Iervolino et al., 2011). Per tant, considerar el TOC com una entitat unitària podria enfosquir els resultats dels estudis que intenten comprendre els mecanismes psicològics i biològics implicats en el trastorn i obstaculitzar el progrés en el desenvolupament de noves estratègies de tractament (Iervolino et al., 2011). Un enfocament que consideri adequadament la heterogeneïtat de la malaltia, així com el marc de desenvolupament, millorarà la

nostra comprensió del TOC i permetrà el reconeixement de fenotips més refinats en futurs estudis examinant l'etiologia, fisiopatologia i el tractament per al TOC. A continuació es mencionaran algunes àrees de recerca prometedores que tenen el potencial d'avançar el nostre coneixement en aquest àmbit.

- Perfeccionament dels instruments d'avaluació disponibles:

Existeix la necessitat de comptar amb instruments clínics psicomètricament robustos que siguin capaços de mesurar tant la gravetat global del TOC com les seves principals dimensions de símptomes (Pertusa et al., 2012). L'escala Dimensional Y-BOCS (DY-BOCS) (Rosario-Campos et al., 2006) es va desenvolupar per a satisfer aquestes necessitats. Malauradament, aquest instrument no estava disponible en el moment en que els estudis actuals es van dissenyar. Estudis futurs també podrien beneficiar-se de mètodes multi-informats de la mesura de símptomes, com ara la combinació d'auto-informe amb l'informe dels pares i els clínics per tal de captar de manera més completa la globalitat dels símptomes dels pacients. Això pot ser especialment rellevant en els nens més petits que no són capaços de proporcionar un auto-informe precís dels seus símptomes.

- Estudis longitudinals, genètics i d'imatge:

Es necessiten més estudis longitudinals (i de més llarga durada) que examinin les variacions en els símptomes obsessivocompulsius, els patrons de comorbiditat, els circuits cerebrals involucrats i els factors de risc ambientals, sobretot si aquests factors es vinculen amb la possibilitat d'explorar els potencials determinants genètics lligats als símptomes (Leckman et al., 2009). Igualment, els estudis de bessons i de famílies han demostrat ser especialment útils per aclarir l'estructura causal subjacent a les dimensions dels símptomes i la naturalesa heterogènia del TOC (Iervolino et al., 2011; van Grootheest, Bartels, et al., 2007; van Grootheest, Cath, et al., 2007). També es necessita més recerca centrada en la detecció dels loci de susceptibilitat genètica que poden contribuir a l'expressió de la variada simptomatologia obsessivocompulsiva (Leckman et al., 2009). De la mateixa manera, els estudis de neuroimatge funcional tenen el potencial de proporcionar una validació addicional de l'enfocament dimensional del TOC (Lawrence et al., 2007; Mataix-Cols, Wooderson, et al., 2004). En els propers anys es preveu que noves investigacions ajudin a traçar un mapa més precís dels sistemes neurals comuns i diferencials implicats en cadascuna de les dimensions principals del TOC.

- Implicacions per al tractament:

Respecte al tractament, serien necessàries més investigacions per tal d'assegurar-se que el coneixement acumulat sobre el TOC i els mecanismes subjacents a aquesta condició es tradueix en intervencions terapèutiques eficaces. Idealment, aquestes intervencions haurien d'adaptar-se a les dimensions específiques, diferents poblacions, i diferents etapes del desenvolupament (Marques et al., 2010; Sookman et al., 2005; Steketee et al., 2001). No obstant això, en aquest sentit segueix existint una considerable marge de millora.

- Trastorns relacionats amb el TOC:

El model multidimensional de TOC i l'estudi dels seus fenotips d'acord amb els mètodes descrits anteriorment no només ha portat a la conceptualització de TOC com una condició heterogènia, sinó també a un refinament de la seva nosologia. L'exemple més obvi d'això és l'acumulació, que ha estat sempre considerada un símptoma (o una dimensió) del TOC i, gràcies a la recerca portada a terme en els darrers 10 anys, i tot i que en ocasions també es pot trobar en el context del TOC, ara es classifica com una entitat independent anomenada "Trastorn d'Acumulació". Aquest nou trastorn s'inclou en el recentment publicat DSM-5 dintre del nou capítol de *Trastorns Obsessivocompulsiu i Afins* (American Psychiatric Association, 2013; Mataix-Cols et al., 2010).

La relació entre el TOC i altres trastorns relacionats amb el TOC (p. ex., Trastorn Dismòrfic Corporal o Tricotilomania) també segueix sent una àrea poc investigada. Un estudi més profund de tots els trastorns de l'espectre obsessivocompulsiu i fer esforços per aclarir els patrons de comorbiditat i l'etiologia compartida entre ells tindria importants implicacions clíniques per als mètodes d'avaluació i tractament, així com per guiar la recerca futura.

CONCLUSIONS

Els objectius d'aquesta tesi van ser estudiar característiques no explorades fins ara del TOC pediàtric, tenint en compte l'heterogeneïtat clínica del trastorn, en una mostra gran de nens i adolescents amb TOC. Els estudis es van focalitzar en 1) l'estudi de l'estabilitat temporal dels símptomes i les dimensions de símptomes obsessivocompulsius en nens i adolescents i 2) en explorar les característiques i la resposta al tractament de les obsessions sexuals en aquest grup d'edat.

Les conclusions principals d'aquesta tesi, derivades de l'*Estudi 1* (I, II, III) i l'*Estudi 2* (IV, V, VI), així com la importància dels resultats (VII) i línies futures de recerca que es podrien desenvolupar (VIII) es poden resumir en els següents punts:

I. El contingut dels símptomes i les dimensions de símptomes del TOC en nens i adolescents és relativament estable al llarg del temps i s'expandeix fins a l'edat adulta primerenca.

II. Altres variables addicionals, com ara l'edat d'inici del TOC o la gravetat dels símptomes, no semblen tenir un efecte sobre l'estabilitat de les dimensions de símptomes.

III. La majoria dels canvis que es produeixen en els símptomes ho fan dins i no entre les dimensions de símptomes i són en gran part atribuïbles a la remissió clínica.

IV. Al voltant d'un de cada quatre nens i adolescents amb TOC presenten obsessions sexuals. Aquestes obsessions són més comunes en els adolescents, però també poden estar presents en pacients prepuberals.

V. Les obsessions sexuals s'associen amb determinades característiques clíniques com la presència de més símptomes depressius i TOC lleugerament més greu.

VI. La presència d'obsessions sexuals no interfereix amb la resposta al tractament amb TCC (amb o sense medicació).

VII. Els resultats d'ambdós estudis reforcen la conceptualització de TOC com una entitat fenotípicament heterogènia que es manifesta d'aquesta manera al llarg de tots els estadis de desenvolupament.

VIII. Futures línies de recerca que, sota aquest enfocament, tenen el potencial d'avançar el coneixement del TOC i els seus trastorns relacionats inclouen: 1) el perfeccionament dels instruments d'avaluació, 2) estudis longitudinals, genètics i de neuroimatge en mostres més grans, i 3) adaptar els tractaments a dimensions específiques, poblacions, i etapes del desenvolupament.

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